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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

In re: AVALANCHE BIOTECHNOLOGIES SECURITIES LITIGATION	Master File No. 15-cv-03185-JD CLASS ACTION
This Document Relates To: All Actions	**FIRST AMENDED CONSOLIDATED CLASS ACTION COMPLAINT** **DEMAND FOR JURY TRIAL**

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TABLE OF DEFINED TERMS AND ABBREVIATIONS

TERM	DEFINITION
2014 Prospectus	Avalanche's prospectus filed pursuant to its IPO on July 31, 2014
2014 Registration Statement or 2014 RS	Avalanche's registration statement no. 333-197133 declared effective by the SEC on July 30, 2014 and 2014 Prospectus incorporated therein.
2015 Prospectus	Avalanche's prospectus filed pursuant to its secondary offering on January 7, 2015
2015 Registration Statement or 2015 RS	Avalanche's registration statement no. 333-201032 declared effective by the SEC on January 7, 2015 and 2015 Prospectus incorporated therein.
AAV	Adeno-Associated Virus
AE	Adverse Event
AMD	Age-related Macular Degeneration
April 2014 Abstract	Elizabeth P Rakoczy, et al., *One Year Follow-Up Report on the rAAV.sFlt-1 Phase I Gene Therapy Trial for Exudative Age-Related Macular Degeneration*, 55 IOVS 1309 (2014)
AR	Adverse Reaction
ARVO	Association for Research in Vision and Ophthalmology
ASCGT	American Society for Cell and Gene Therapy
AVA-101	Avalanche's lead product candidate, an AAV vector intended to treat Wet AMD
AVA-101 Trial	Avalanche's Phase 1/2a trial of AVA-101 in 40 human subjects with Wet AMD
Avalanche	Avalanche Biotechnologies, Inc.
Bain	Linda C. Bain, former CFO of Avalanche
Barone	Samuel Barone, M.D., CMO of Avalanche
BCVA	Best corrected visual acuity
Blumenkranz	Mark S. Blumenkranz, M.D., Chairman of Avalanche's Board of Directors

CEO	Chief Executive Officer
CFO	Chief Financial Officer
CFP	Color fundus photography
Chalberg	Thomas W. Chalberg, Jr., Ph.D., former CEO of Avalanche
Class Period	July 31, 2014 to June 15, 2015
CMO	Chief Medical Officer
CNV	choroidal neovascularization
Constable	Ian J. Constable AO, researcher at LEI and Chairperson of Avalanche's Clinical Advisory Board
Cowen	Cowen & Co., LLC
CTN Form	Notification of Intent to Conduct a Clinical Trial form
DMC	Data Monitoring Committee
ETDRS	Early Treatment Diabetic Retinophathy Study scale
Exchange Act	Securities Exchange Act of 1934
Exchange Act Defendants or EADS	Avalanche, Bain, Blumenkranz, Chalberg, and Schwartz
Exchange Act Plaintiff or EAP	Arpan Bachhawat
FA	Fluorescein Angiography
FDA DMC Guidance	U.S. Food and Drug Administration, Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees, §2.1 (2006)
FDA Safety Reporting Guide	U.S. Food and Drug Administration, Guidance for Industry and Investigators: Safety Reporting Requirements for INDS and BA/BE Studies, at 13 (2012)
Gasmi	Mehdi Gasmi, Senior Vice President of Pharmaceutical Development
HREC	Human and Research Ethics Committee
Hull	Hans Hull, Avalanche's Senior Vice President of Business Operations
ICH E9 Guidance	International Conference on Harmonization (ICH) guidance, E9 Statistical Principles for Clinical Trials,

	§4.5 (1998)
Individual Exchange Act Defendants or IEADs	Bain, Blumenkranz, Chalberg, and Schwartz
Individual Securities Act Defendants or ISADs	Bain, Blumenkranz, Chalberg, McLaughlin, Schwartz, and Wachter
IOP	Intraocular Pressure
IOVS	Investigative Ophthalmology & Visual Science
IPO	Avalanche's Initial Public Offering conducted on or around July 31, 2014
Jefferies	Jefferies, LLC
Lai	Dr. Chooi-May Lai
LEI	Lions Eye Institute
McLaughlin	John P. McLaughlin, director on Avalanche's Board of Directors
NHMRC	National Health and Medical Research Counsel
Piper Jaffray	Piper Jaffray & Co.
Rakoczy	Elizabeth Rakoczy, MSc, Ph.D., researcher at LEI and Chairperson of Avalanche's Scientific Advisory Board
Retina Today Article	*Ocular Gene Therapy Showed Fewer Injections Needed, Increased Visual Gain*, Retina Today (2014)
Safety Surveillance Article	*Optimizing Safety Surveillance During Clinical Trials Using Data Visualization Tools*, Drug Discovery & Development (Oct. 6, 2015, 10:23 AM)
Schwartz	Steven W. Schwartz, M.D., director on Avalanche's Board of Directors
SD-OCT	Spectral Domain Optical Coherence Tomography
SEC	Securities and Exchange Commission
Securities Act	Securities Act of 1933
Securities Act Defendants or SADs	Avalanche, Bain, Blumenkranz, Chalberg, McLaughlin, Schwartz, Wachter, Cowen & Co., Jefferies, Piper Jaffray, and William Blair
Securities Act Plaintiff or SAP	Srikanth Koneru
TGA	Therapeutic Goods Administration

TGA GCP Guide	Therapeutic Goods Administration, *Note for Guidance on Good Clinical Practice*, §5.16.1 (2000)
TGA Pharmacovigilance Requirements	Therapeutic Goods Administration, *Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines*, §2.3.2 (2014)
Trial Overview	Overview of the trial protocol for Avalanche's Phase 1/2a trial of AVA-101 in 40 human subjects with Wet AMD filed on www.clinicaltrials.gov
Underwriter Defendants	Cowen & Co., Jefferies, Piper Jaffray, and William Blair
VEGF	Vascular endothelial growth factor
Wachter	Paul D. Wachter, director on Avalanche's Board of Directors
William Blair	William Blair & Company, LLC

GLOSSARY

TERM	DEFINITION
Adeno-Associated Virus (AAV)	A harmless, small virus that infects most humans and does not instigate an immune response.
Adverse Event	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
Adverse Reaction	Any noxious and unintended response to a medicinal product related to any dose meaning that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.
Antibody	Proteins in the blood that are recruited by the immune system to identify and neutralize foreign objects like bacteria and viruses.
AVA-101	A vector to deliver and express a function gene to eye cells to promote continuous protein production, a/k/a AAV.sFlt1"
Baseline Data	Data collected at the beginning of a clinical study for all participants.
Best Corrected Visual Acuity (BCVA)	Visual acuity measure after corrective tool or treatment is used.
Biomicroscopy	Standard examination of the eye using a slit-lamp and magnifying lens.
Choroid	The vascular layer of the eye, containing connective tissue. It makes up part of the uvea layer of the eye which sits underneath the retina.
Choroidal Neovascularization (CNV)	The creation of new blood vessels in the choroid layer of the eye which is one layer beneath the retina.
Color Fundus Photography (CFP)	Color photographs taken of the retina.
Early Treatment Diabetic Retinopathy Study Scale (ETDRS)	A standard eye chart used to test visual acuity characterized by 5 roman letters per row with rows descending in size.

Fluorescein Angiography (FA)	A medical procedure where fluorescent dye is injected into the blood stream and then the dye highlights the blood vessels in the back of the eye so they can be photographed.
Fovea	The center of the macula that forms a small pit and contains the largest concentration of cone cells in the eye making it responsible for central, high-resolution vision.
Foveal Thickness	Retinal thickness
Human and Research Ethics Committee (HREC)	Committees affiliated with organizations that conduct research on humans. The TGA requires all clinical trials of unregistered therapeutic goods to be reviewed and monitored by an HREC.
Indirect Ophthalmoscopy	Standard examination of the interior of the eye using a headband with a light attached and small hand-held lens.
Intraocular Pressure (IOP)	Fluid pressure inside the eye caused by an excess of aqueous fluid.
Intravitreal Injection	Injection to the jelly-like fluid in the center of the eye.
Investigational New Drug Application (IND)	A request for Food and Drug Administration authorization to administer a drug under clinical development to humans.
Macula	An oval-shaped pigmented area near the center of the retina which is responsible for central vision.
Ocular Inflammation	Swelling of the uvea layer of the eye that sits underneath the retina.
Open-Label Trial	The type of clinical trial where both the investigators and the subjects know whether placebo or treatment is being administered.
Opthalmic Safety	Safety relating to the eye.
Pharmacovigilance	All scientific and data gathering activities relating to the detection, assessment, and understanding of adverse events or adverse reactions.
Primary Endpoint	Measures the outcome that will answer the primary (or

	most important) question being asked by a trial, such as whether a new treatment is better at preventing disease-related death than the standard therapy.
rAAV.sFlt-1	AVA-101
Ranibizumab	Current treatment of Wet AMD marketed by Genetech, Inc. under the name "Lucentis."
Rescue Injection	Additional subretinal injection of ranibizumab
Retina	The light-sensitive layer at the back of the eye that covers about 65 percent of the interior surface of the eye.
Secondary Endpoint	Measures relevant questions being asked by a clinical trial in addition to the primary endpoint.
sFLT-1	The naturally-occurring anti-VEGF protein found in AVA-101.
Spectral Domain Optical Coherence Tomography (SD-OCT)	A non-contact medical imaging technology where reflected light is used to produce detailed cross-sectional and 3D images of the eye.
Statistical Significance	The likelihood that a relationship or result is caused by something other than mere random chance. Statistical hypothesis testing is employed using a "p-value" representing the probability that random chance could explain the result. A p-value of less than 5% is usually considered statistically significant.
Subretinal Injection	Injection into the retinal layer of the eye.
Therapeutic Goods Administration (TGA)	The regulatory body for therapeutic goods (including medicines, medical devices, gene technology, and blood products) in Australia.
Trial Protocol	A document that describes how a clinical trial will be conducted (the objective(s), design, methodology, statistical considerations and organization of a clinical trial,) and ensures the safety of the trial subjects and integrity of the data collected.
Um	The International System of Units' symbol for a micrometer or microns.

Vascular Endothelial Growth Factor (VEGF)	A signal protein produced by cells to stimulate the creation of blood cells to restore the oxygen supply to tissues when blood flow is inadequate.
Viral Vector	Virus cell that has had the disease-causing genes removed and is then inserted into the body to transfer desired genes to targeted cells by infecting those cells.
Visual Acuity	The clearness or sharpness of vision measured at a distance of 20 feet.
Vitreous Cavity	The center cavity of the eye behind the lens that is filled with vitreous gel.
Wet Age-Related Macular Degeneration (Wet AMD)	Disease of the eye whereby blood vessels form in the macula causing bleeding, leakage, and scarring in the retina and distorting central vision.

CHRONOLOGY OF KEY EVENTS

DATE	EVENT
December 14, 2011	The Trial Overview for the AVA-101 Trial is filed on www.clinicaltrials.gov
January 2012	The first patients begin to enroll in Phase 1 of the AVA-101 Trial
April 2012	Phase 1 of the AVA-101 Trial has been fully enrolled
April 2012	Enrollment begins for Phase 2a of the AVA-101 Trial
May 3, 2012	The 8-week safety results for Phase 1 of the AVA-101 Trial are published
December 31, 2012	12 patients have enrolled in Phase 2a of the AVA-101 Trial
May 2013	A progress report for Phase 1 of the AVA-101 Trial is published
June 2013	Safety data for the first 17 patients enrolled in the AVA-101 Trial is published
December 31, 2013	30 patients have enrolled in Phase 2a of the AVA-101 Trial
February 8, 2014	Phase 2a of the AVA-101 Trial has been fully enrolled
April 2014	The April 2014 Abstract is published announcing the Phase 1 results
April 8, 2014	8-week results from all Phase 2a patients available
May 5, 2014	The April 2014 Abstract is presented at the ARVO meeting discussing the Phase 1 1-year results
May 9, 2014	LEI publishes a media statement discussing the Phase 1 results
June 2014	Avalanche reviews interim safety surveillance data
July 15, 2014	Ophthalmology Times publishes an article discussing the Phase 1 1-year results
July 31, 2014	Avalanche's IPO commences
January 7, 2015	Avalanche's secondary offering commences
January 16, 2015	An analyst report states that the Company saw the Phase 2a data
June 15, 2015	The Phase 2a topline results are announced
June 16, 2015	Avalanche's common stock closes at $17.05 per share, 56% lower than the previous trading day
July 23, 2015	Chalberg resigns as CEO of Avalanche

August 13, 2015	Avalanche announces its plan to stop clinical development of AVA-101
October 19, 2015	Bain resigns as CFO of Avalanche

The allegations in this First Amended Consolidated Class Action Complaint are based on the personal knowledge of Lead Plaintiff Arpan Bachhawat ("**Bachhawat**") and Plaintiff Srikanth Koneru ("**Koneru**") (collectively "**Plaintiffs**") as to Plaintiffs' own acts, and are based upon information and belief as to all other matters alleged herein. Plaintiffs' information and belief is based upon the investigation by Plaintiffs' counsel into the facts and circumstances alleged herein, including, (i) review and analysis of those public filings Avalanche Biotechnologies, Inc. ("**Avalanche**" and the "**Company**") made with the United States Securities and Exchange Commission ("**SEC**") referenced herein; (ii) review and analysis of those press releases, analyst reports, public statements, news articles and other publications referenced herein disseminated by or concerning Avalanche and the other defendants named herein (together with Avalanche, the "**Defendants**"); (iii) review and analysis of those Company conference calls, press conferences, and related statements and materials referenced herein; and (iv) review and analysis of those other documents referenced herein. Many additional facts supporting the allegations are known only to Defendants and/or are within their exclusive custody or control and/or in the custody and control of the U.S. Food and Drug Administration ("**FDA**") or Australian Therapeutic Goods Administration ("**TGA**"). Plaintiffs believe that additional evidentiary support for their allegations will emerge after a reasonable opportunity to conduct discovery.

Plaintiffs respectively assert two separate sets of claims in this Complaint. In Counts One and Two, Koneru asserts strict-liability claims under Sections 11 and 15 of the Securities Act of 1933 against Avalanche; Chalberg; Bain; Blumenkranz; Schwartz; John P. McLaughlin ("**McLaughlin**"); Paul D. Wachter ("**Wachter**"); Jefferies LLC ("**Jefferies**"); Cowen & Co., LLC ("**Cowen**"); Piper Jaffray & Co. ("**Piper Jaffray**"); and William Blair & Co. ("**William Blair**"). Koneru expressly disclaims any allegations of fraud in these non-fraud claims brought under the Securities Act. In Counts Three and Four, Bachhawat asserts fraud claims under Sections 10(b) and 20(a) of the Exchange Act of 1934 against Avalanche; Chalberg; Linda C. Bain ("**Bain**"); Blumenkranz; and Schwartz.

Plaintiffs, respectively, bring this federal class action on behalf of purchasers of publicly traded Avalanche common stock who (1) purchased Avalanche common stock pursuant or traceable to Avalanche's IPO, defined herein, and were damaged thereby, seeking to pursue remedies under Sections 11 and 15 of the Securities Act of 1933 ("**Securities Act**") and/or (2) purchased Avalanche common stock between July 31, 2014 and June 15, 2015, inclusive (the "**Class Period**"), and were damaged thereby, seeking to pursue remedies under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (the "**Exchange Act**"), and Rule 10b-5 promulgated thereunder (together the "**Class**").

JURISDICTION AND VENUE

1. This action arises under and pursuant to Sections 11 and 15 of the Securities Act (15 U.S.C. §§ 77k and 77o), and Sections 10(b) and 20(a) of the Exchange Act, (15 U.S.C. §§ 78j(b) & 78t(a)), and SEC Rule 10b-5 promulgated thereunder by the SEC (17 C.F.R. § 240.10b-5).

2. This Court has jurisdiction over the action pursuant to 28 U.S.C. § 1331, Section 22 of the Securities Act (15 U.S.C. § 77v), and Section 27 of the Exchange Act (15 U.S.C. § 78aa).

3. Venue is proper in this District pursuant to 28 U.S.C. § 1391(b) and Section 27 of the Exchange Act (15 U.S.C. § 78aa). Avalanche maintains its principal place of business in this District.[1] Certain of the acts and conduct complained of herein, including dissemination of materially false and misleading information to the investing public, occurred in this District.

4. In connection with the acts alleged in this Complaint, Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce, including, but not limited to, the mails, interstate telephone communications, and the facilities of the national securities markets.

CLASS ACTION ALLEGATIONS—APPLIES TO BOTH SETS OF CLAIMS

5. Plaintiffs bring this action pursuant to Rule 23(a) and 23(b)(3) of the Federal Rules of Civil Procedure on behalf of themselves and all persons and entities who purchased Avalanche

[1] Although it is now known as Adverum Biotechnologies, Inc., because the Company was re-named after the relevant time period, it will be referred to herein solely as Avalanche.

common stock pursuant or traceable to the Avalanche IPO, defined herein, and were damaged thereby, seeking to pursue remedies under the Securities Act and/or purchased Avalanche common stock between July 31, 2014 and June 15, 2015, inclusive, and were damaged thereby, seeking to pursue remedies under the Exchange Act and Rule 10b-5 promulgated thereunder.

6. Excluded from the Class are Defendants named herein, members of their immediate families, any firm, trust, partnership, corporation, officer, director or other individual or entity in which a Defendant has a controlling interest or which is related to or affiliated with any Defendants (defined below), and the legal representatives, heirs, successors-in-interest or assigns of such excluded persons.

7. The members of the Class are so numerous that joinder of all members is impracticable. During the relevant time period, Avalanche common stock was actively traded on the NASDAQ Global Select Market, which is an efficient market. While the exact number of Class members cannot be determined at this early stage and can only be ascertained through appropriate discovery, Plaintiffs believe that the proposed Class numbers in the thousands. Record owners and other members of the Class may be identified from records maintained by Avalanche or its transfer agent and may be notified of the pendency of this action by mail, using a form of notice similar to that customarily used in securities class actions.

8. Plaintiffs' claims are typical of the claims of the other members of the Class. All members of the Class were similarly affected by Defendants' allegedly wrongful conduct in violation of the Exchange Act and/or Securities Act as complained of herein.

9. Plaintiffs will fairly and adequately protect the interests of the Class and have retained counsel competent and experienced in class action and securities litigation. Plaintiffs have no interests that are contrary to or in conflict with those of the Class.

10. Common questions of law and fact exist as to all members of the Class, and predominate over any questions solely affecting individual members of the Class. The questions of law and fact common to the Class include, inter alia:

a) whether the federal securities laws were violated by Defendants' acts as alleged herein;

b) whether statements made by Defendants during the relevant time period contained untrue statements of material fact and/or omitted to state material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading;

c) whether and to what extent the market price of Avalanche's common stock was artificially inflated during the Class Period because of the material misrepresentations made herein;

d) whether the Exchange Act Defendants acted with the requisite scienter with respect to the Exchange Act claims;

e) whether the Individual Defendants were controlling persons of Avalanche;

f) whether reliance may be presumed pursuant to the *Affiliated Ute* presumption on fraud-on-the-market presumption for the Exchange Act Claims; and

g) whether the members of the Class have sustained damages as a result of the conduct complained of herein and, if so, the proper measure of damages.

11. Plaintiffs know of no difficulty that will be encountered in the management of this action that would preclude its maintenance as a class action.

12. A class action is superior to all other available methods for the fair and efficient adjudication of this action because, among other things, joinder of all members of the Class is impracticable. In addition, since the damages suffered by individual members of the Class may be relatively small, the expense and burden of individual litigation would make it nearly impossible for members of the Class to bring individual actions.

SECURITIES ACT CLAIMS

13. At the beginning of 2012, with the help of its Australian trial investigator, the Lion's Eye Institute ("**LEI**"), Avalanche embarked on a clinical trial program to test its novel gene therapy, AVA-101, in patients with Wet AMD. While the current standard of care for Wet AMD

required injections into the eye every 4 to 8 weeks in order to maintain stable vision, AVA-101 was designed to be a one-time genetic cure for the disease. However, in order to function properly, AVA-101 had to be administered through an invasive sub-retinal injection which was significantly more invasive than administration of the standard therapies, requiring an operation and anesthesia, and thus was subject to far more complications than the intravitreal injection required by the standard therapies. In order for AVA-101 to be a worthwhile treatment for Wet AMD and to justify the risks of the more invasive procedure, AVA-101 needed to be significantly more effective than the current treatment.

14. The clinical trial of AVA-101 in patients with Wet AMD (the "**AVA-101 Trial**" or the "**Trial**") was broken into two phases. Phase 1 involved 8 patients and was fully enrolled by April 2012, and Phase 2a involved 32 patients and began enrollment in April 2012. The Trial was open-label, meaning that the results were not blinded to the parties involved, and its primary endpoint was ocular safety. The Trial's secondary endpoint was efficacy, although the Trial was ***not*** powered to show statistical significance as to efficacy.

15. Phase 2a of the Trial was designed to span one year. On the first week of the Trial patients in the treatment arm were to receive a subretinal injection of AVA-101, and thereafter, beginning on the eighth week of the trial, study visits were to occur every 4 weeks through wee 52. During these follow-up visits patients in both the treatment arm and the control arm were eligible to receive injections of the standard therapy, *i.e.* "rescue injections," if their Wet AMD symptoms materially worsened.

16. Rescue injections were provided to patients when pre-specified criteria for any one of the following were reached: vision decreased, retinal thickening was observed, or retinal fluid leakage was detected. These three measures, along with the number of rescue injections required, were not only the efficacy endpoints for the trial, but they were also measured by the same methods that were used to observe ocular safety, the safety endpoint for the Trial. Therefore, the safety data would also have indicated whether AVA-101 was effective in patients.

17. As patients progressed through Phase 2a of the Trial, data from each monthly visit was entered and compiled in a database as part of the safety surveillance program required by federal regulation. This data was periodically reviewed by the Trial's safety data monitoring committee; indeed in June 2014, an interim analysis was conducted.

18. By February 8, 2014, Phase 2a of the AVA-101 Trial was fully enrolled. Two months later, Avalanche and LEI began to publicize the remarkable 52-week results from the 8 patients enrolled in Phase 1 of the AVA-101 Trial. The results showed that in Phase 1, AVA-101 had the desired effect in the treatment arm as on average ***retinal thickness decreased by 200 um***,[2] ***visual acuity increased by 7.5 letters***, and ***5 of 6 patients in the treatment arm did not receive any rescue injections***, as ***out of a possible 72 rescue injections, only 2 rescue injections were given***. These results provided hope that one subretinal injection of AVA-101 may cure Wet AMD because nearly every patient was able to maintain stable vision without the need for a rescue injection for an entire year.

19. In the aftermath of the exceptional Phase 1 results, Avalanche launched its initial public offering ("**IPO**") on July 30, 2014, issuing 6.9 million shares and raising $106.8 million, after deducting underwriting discounts and commissions and estimated offering expenses. At this time, sufficient data existed to indicate that AVA-101 was not having the desired effect in patients in Phase 2a of the Trial. Specifically, within the first 8 weeks of treating patients in Phase 2a, data showed that retinas were thickening for patients in the treatment arm and thinning for patients in the control arm by a difference of 81 um—the opposite of what you would see with an effective drug—and this delta remained constant throughout the Trial. Also, the full 1-year data would have most likely been available for 22 of 32 patients by July 2014; 7-month or greater data would have been available for the remaining 8 patients enrolled in the latter half of 2013; and 5-month or greater data would have been available for the 2 patients who enrolled in 2014. This amount of data would have been sufficient to indicate that the retinas of patients in the treatment group were thickening and

[2] "Um" is the International System of Units' symbol for a micrometer or microns. *See Micrometre*, Wikipedia, https://en.wikipedia.org/wiki/Micrometre (last visited Dec. 1, 2016).

patients in the treatment arm were receiving rescue injections at a materially greater rate than patients in Phase 1 of the Trial. Thus revealing that AVA-101 was not a material improvement over the standard of care and would not justify the more invasive procedure it entailed.

20. The offering documents failed to disclose the uncertainties created by this trend of adverse trial data and the true risks arising from this adverse Trial data. Indeed, this data was not revealed to the public until June 15, 2015.

21. On June 15, 2015, Avalanche announced the one-year results from Phase 2a of the AVA-101 Trial and ultimately had to admit that the Trial showed that AVA-101 was not effective in treating Wet AMD. The results revealed that in many cases, the patients in the treatment arm fared worse than those in the control arm. Indeed, the retinas of the treatment arm thickened by 25 um whereas the retinas of the control arm thinned by 56 um. The treatment arm received an average of 3.1 rescue injections, with 47% of patients receiving between 3 and 7 rescue injections, whereas the control arm received an average of 3.6 rescue injections, with patients receiving between 2 and 5 rescue injections. These results were an utter failure compared to Phase 1 of the Trial where 5 of 6 patients received 0 rescue injections and retinal thickness decreased in the treatment group by 200 um. Thus, the Phase 2a results did not justify the heightened risks of subretinal injection.

22. The results from Phase 2a were not well received by the market. Two analysts cut their price projections for the Company by more than half, and several other investor publications criticized the results, with one going so far as to state that "I'm struggling to adequately describe the awfulness of Avalanche Biotechnologies' [] performance Monday night[.]" On these results, the stock plummeted more than 56%, closing on June 16, 2015 at $17.05 per share.

23. Several months later, Avalanche was forced to face the facts and decided to abandon development of AVA-101 based upon the lack of efficacy shown in Phase 2a of the Trial. Indeed, the results were so poor that further development was not warranted even though Phase 2a was not powered to show statistical significance of efficacy.

24. As set forth more fully below, the true facts, which existed at the time the Company filed its Registration Statement but were not disclosed to the public, were that:

a) patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening of the retina, evidencing that AVA-101 was not effective in treating Wet AMD;

b) patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD; and

c) as a result, Avalanche's business and financial prospects concerning AVA-101 were not what the marked was informed.

I. SECURITIES ACT PARTIES

A. The Securities Act Plaintiff

25. Plaintiff Srikanth Koneru purchased 71 shares of Avalanche common stock at $25.81 per share on July 31, 2014 and was damaged thereby. Plaintiff still holds all of his shares as of the date of the filing of this Complaint. Plaintiff Koneru is referred to herein as the "**Securities Act Plaintiff**."

B. The Securities Act Defendants

1. The Company

26. Defendant Avalanche was a Delaware corporation with its principal executive offices located at 1035 O'Brien Drive, Suite A, Menlo Park, California 94025. Avalanche was a biopharmaceutical company that used its proprietary Ocular BioFactory™ platform to discover and develop novel treatments for ophthalmic diseases. During the relevant time period, the Company's stock was traded on the NASDAQ Global Select Market ("**NASDAQ**") under the symbol "AAVL."

2. The Individual Securities Act Defendants

27. Defendant Chalberg co-founded Avalanche, and was until his resignation on July 23, 2015, Chief Executive Officer ("**CEO**"), president, and a member of the Board of Directors of Avalanche. Chalberg signed the 2014 Registration Statement (defined below) in connection with the IPO. Chalberg directly participated in and controlled the management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

28. Defendant Bain was the Chief Financial Officer ("**CFO**") of Avalanche until her resignation on October 19, 2015. Defendant Bain signed the 2014 Registration Statement in connection with the IPO. Bain directly participated in and controlled the management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

29. Defendant Blumenkranz co-founded Avalanche and was at all relevant times the Chairman of the Board of Directors of Avalanche. Defendant Blumenkranz signed the 2014 Registration Statement in connection with the IPO. Blumenkranz directly participated in and controlled the management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

30. Defendant Schwartz co-founded Avalanche and was at all relevant times a member of Avalanche's Board of Directors. Defendant Schwartz signed the 2014 Registration Statement in connection with the IPO. Schwartz directly participated in and controlled the management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

31. Defendant McLaughlin was at all relevant times a member of Avalanche's Board of Directors. Defendant McLaughlin signed the 2014 Registration Statement in connection with the IPO. McLaughlin directly participated in and controlled management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

32. Defendant Wachter was at all relevant times a member of Avalanche's Board of Directors. Defendant Wachter signed the 2014 Registration Statement in connection with the IPO. Wachter directly participated in and controlled management of the Company, including, without limitation, the publication of the 2014 Registration Statement.

33. The defendants listed in ¶¶27-32 are collectively referred to herein as the "**Individual Securities Act Defendants**."

3. The Underwriter Defendants

34. Defendant Jefferies acted as an underwriter of the IPO. Jefferies is headquartered at 520 Madison Avenue, 10th Floor, New York, NY 10022.

35. Defendant Cowen acted as an underwriter of the IPO. Cowen is headquartered at 599 Lexington Avenue, New York, NY 10022.

36. Defendant Piper Jaffray acted as an underwriter of the IPO. Piper Jaffray is headquartered at 800 Nicollet Mall, Suite 1000, Minneapolis, MN 55402.

37. Defendant William Blair acted as an underwriter of the IPO. William Blair is headquartered at 222 West Adams Street, Chicago, IL 60606.

38. The defendants enumerated in ¶¶34-37 are collectively referred to herein as the "**Underwriter Defendants**."

39. The Company, the Individual Securities Act Defendants, and the Underwriter Defendants are collectively referred to herein as the "**Securities Act Defendants**."

40. Pursuant to the Securities Act, the Underwriter Defendants are liable for the false and misleading statements in the 2014 Registration Statement. Representatives of the Underwriter Defendants assisted Avalanche and the Individual Securities Act Defendants in planning the IPO and purportedly conducted an adequate and reasonable due diligence investigation into the business and operations of Avalanche. As part of their due diligence investigation the Underwriter Defendants had continuous access to confidential corporate information concerning Avalanche's clinical trials and met with Avalanche's lawyers, management, and top executives. As a result, a reasonable due diligence investigation would have revealed the misleading statements and omissions contained in the 2014 Registration Statement, as detailed herein.

41. The Underwriter Defendants caused the 2014 Registration Statement to be filed with the SEC and declared effective in connection with offers and sales thereof, including to Koneru and other members of the Class who purchased shares traceable to the 2014 Registration Statement, after having failed to disclose the misleading statements and omissions in the 2014 Registration Statement.

II. BACKGROUND OF THE SECURITIES ACT CLAIMS

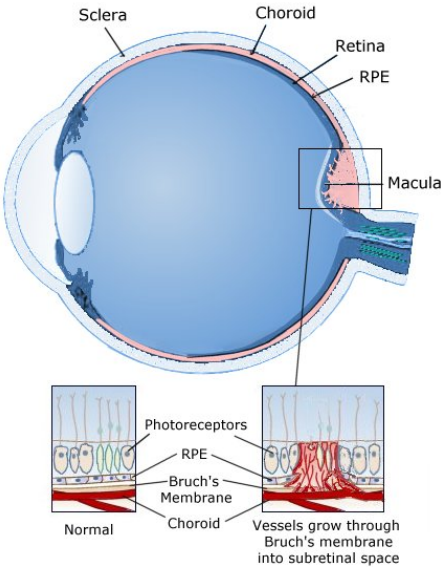
A. Background of the Company, Wet AMD, and AVA-101

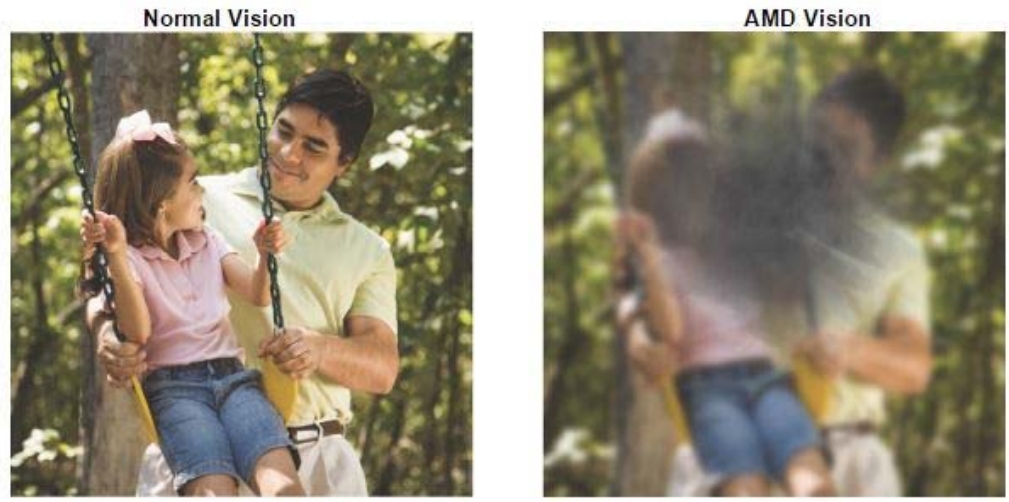
42. Avalanche is a biopharmaceutical company focused on the development and commercialization of a gene therapy platform, dubbed its Ocular BioFactory™ platform, which is designed to treat ophthalmic diseases. *See The Ocular BioFactory™*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/the-ocular-biofactory.php (last visited Jan. 29, 2016). Avalanche's Ocular BioFactory™ platform consists of treatments that use the adeno-associated virus ("**AAV**") as a vector to deliver and express a functional gene to the cells of the eye to promote continuous production of a certain protein. *See id.*

43. Avalanche's lead AAV vector was AVA-101, a/k/a rAAV.sFlt-1, which was being developed to treat Wet AMD. *See* Ex. B, the 2014 Registration Statement. AMD is a progressive disease affecting the cells in the macula, which is an oval-shaped pigmented area that forms the center of the retina and is the region of the eye responsible for central vision. *See About Age-Related Macular Degeneration*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/about-amd.php (last visited Jan. 18, 2016).

44. Wet AMD is an advanced form of AMD whereby patients suffer from debilitating vision loss and loss of the ability to perform daily activities. *See* Salveen Richter, SunTrust Robinson Humphrey, An Eye To a Cure, Initiating with a Buy and $60 PT, 14 (2015). ***Wet AMD occurs when the membrane underlying the retina thickens, then breaks***. *See Wet AMD*, The Macular Degeneration Partnership, https://www.amd.org/what-is-macular-degeneration/wet-amd/ (last visited Jan. 29, 2016). The oxygen supply to the macula is disrupted and the body responds by growing new, abnormal blood vessels, which is known as choroidal neovascularization ("**CNV**"). *See id.*; *see also Wet Macular Degeneration (AMD)*, American Macular Degeneration Foundation, https://www.macular.org/wet-amd (last visited Jan. 29, 2016). These new blood vessels are very fragile and often leak and bleed, which results in excess fluid in the retina causing swelling—*i.e.*, thickening of—the retina. *See Wet AMD*, The Macular Degeneration Partnership, https://www.amd.org/what-is-macular-degeneration/wet-amd/ (last visited Jan. 29, 2016). The

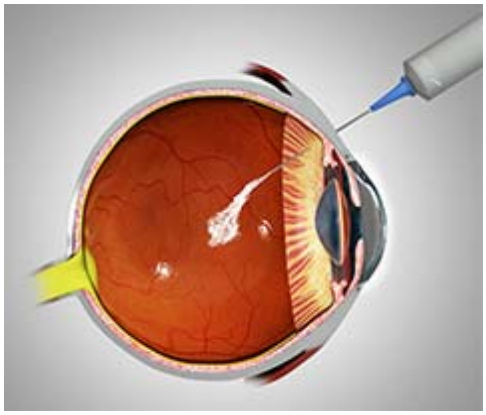
leakage from these blood vessels also damages photo receptors, which results in rapid vision loss. *See id.* A diagram of this process and a demonstration of the type of vision loss experienced are set forth below:





45. Vascular endothelial growth factor ("**VEGF**") is a protein known to play a central role in the growth of the new blood vessels in the retina. *See Current Treatments*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/current-treatments.php (last visited Jan. 18, 2016). A number of FDA-approved therapies have been developed to block the effects of VEGF by binding to and sequestering the protein, causing the new blood vessels to shrink. *See id.* The most common FDA-approved anti-VEGF treatments are (1) Lucentis® (ranibizumab),

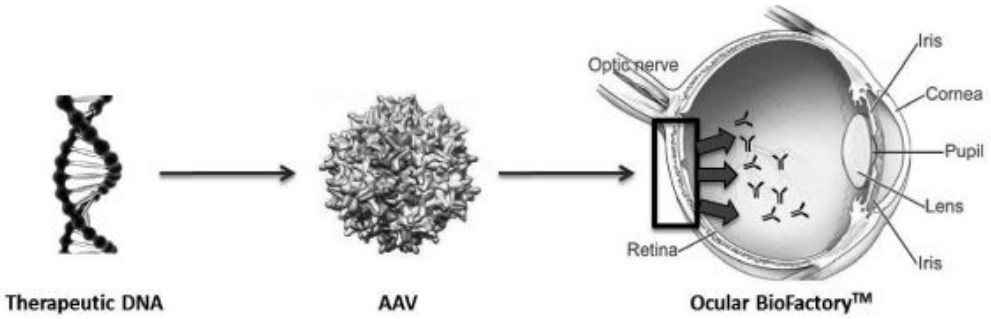
marketed by Genentech, Inc. and Novartis AG, which is an antibody fragment that binds to and inhibits VEGF proteins in the eye; (2) EYLEA®, marketed by Regeneron Pharmaceuticals, Inc., which is a recombinant fusion protein containing portions of the human VEGF receptor that binds to soluble VEGF; and (3) Avastin®, marketed by Genentech, Inc., which is an antibody that binds to VEGF. *See id.* ***These existing treatments are administered through intravitreal injections***, which are injections into the center of the eye after administration of topical anesthesia, depicted as follows:



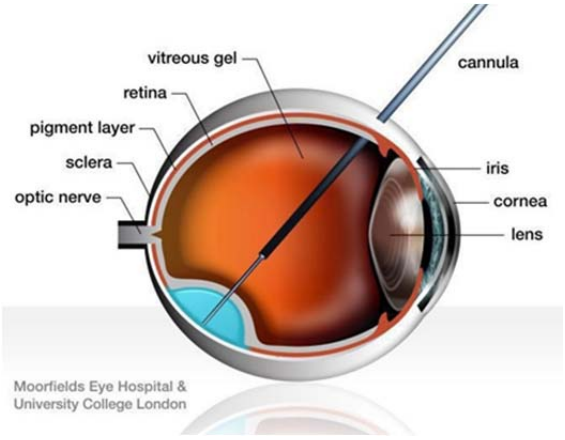
46. Because these biologic agents decay over time, causing "peaks" and "troughs" of VEGF inhibition, ***standard treatments require injections every 4 to 8 weeks*** to maintain stable vision. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 14 (2015). While these therapies have proven to be effective in treating the symptoms of Wet AMD, the frequency and discomfort of administration is burdensome for patients, leading many to terminate treatment or not comply with the prescribed regimen, resulting in vision loss. *See id.*

47. In contrast to the current standards of care, which are laboratory-manufactured antibodies, AVA-101 purported to be a novel gene therapy. This gene therapy utilized a viral vector to carry the desired genetic information—nucleic acids that encode a protein of interest—to target cells and cause them to utilize the cell's machinery to express the protein of interest. *See* Aaron Shapiro, *Gene Therapy for Retinal Diseases*, Retina Today, April 2015, at 24. The goal of

gene therapy is to provide a sustained therapeutic benefit via continual expression of the protein of interest. *See id.* AVA-101 is comprised of the AAV2 vector, which contains a gene encoding sFLT-1, a naturally occurring anti-VEGF protein. *See* 2014 Registration Statement at 81. Avalanche hypothesized that when administered in the eye and expressed by the host retinal cells, the sFLT-1 protein would inhibit the formation of new blood vessels and block VEGF activity. *See id.* A diagram of how AVA-101 was intended to operate in the eye is included below:



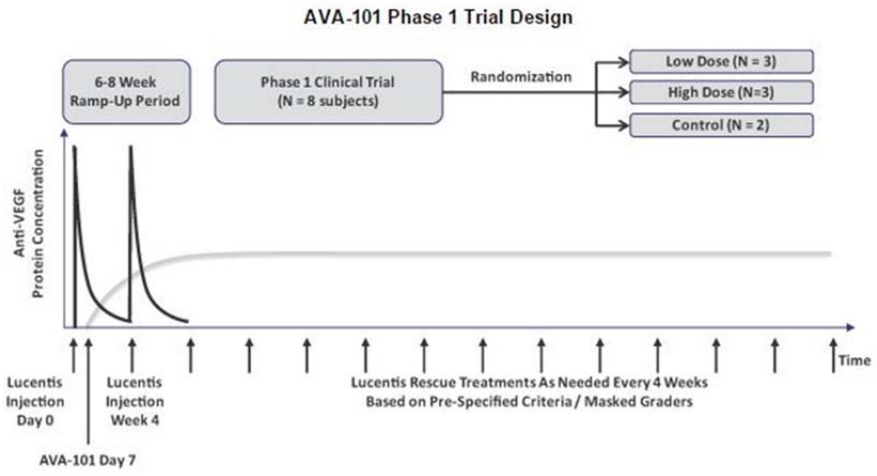
48. ***Unlike the current FDA-approved therapies, AVA-101 was designed to be administered through a single subretinal injection***. *See* 2014 Registration Statement at 81. Subretinal injections are injections through the middle of the eye, directly into the retina in the back of the eye, depicted as follows:



49. The purpose of this type of highly invasive injection is to place the vector in direct contact with the retinal cells to enhance protein expression. *See id.* ***Subretinal injections are more***

difficult to administer and significantly more invasive than intravitreal injections, requiring an operating room and anesthesia. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 23 (2015). ***They are also subject to more adverse safety events*** such as "the development of a retinal hole at the site of entry through the retina, reflux of the therapeutic agent back into the vitreous cavity, potentially decreasing efficacy or scar formation from proliferation of cells on the retinal surface, and prolonged retinal detachment." Biren Amin, Jefferies, *Initiate at Buy: AAVL Gene Therapy Has Disruptive Potential in Wet AMD*, 16-17 (Aug. 25, 2014). Therefore, an analyst at Cowen & Co. stated that "AVA-101 is delivered through a more cumbersome subretinal procedure, and therefore our consultant thinks it needs to either provide meaningfully better efficacy, or result in a significantly diminished subsequent injection burden, in order to be competitive." Phil Nadeau, Cowen & Company, *Ph. IIa Demonstrates Safety and Activity, Though Doesn't Define 101's Role*, 1 (June 16, 2015).

50. If effective, AVA-101 could result in sustained production of a natural inhibitor of VEGF, and therefore stabilize cellular levels of VEGF. ***Thus, a <u>one-time</u> subretinal injection of AVA-101 was designed to introduce a lasting source of VEGF inhibition in the eye and enable constant prevention of new blood vessel formation, eliminating the need for intravitreal injections every 4 to 8 weeks***. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 14 (2015). A graphic of the difference in intended anti-VEGF effect between standard therapies and AVA-101 is as follows:



B. The Phase 1/2a AVA-101 Trial Design

51. Research and development of the science behind AVA-101 began more than 20 years ago, spearheaded by Professor Elizabeth Rakoczy ("**Rakoczy**") at LEI, an ophthalmic research organization based in Perth, Australia. *See* Lions Eye Institute, Annual Report, 34 (2013). Over the years, close to 100 scientists, ophthalmologists, veterinarians, virologists, and PhD students participated in the project. *See id.* From 2002 to 2007 a grant from the National Health and Medical Research Council enabled the research team to take the basic research project to the clinical trial phase. *See id.*

52. LEI began collaborating with Avalanche on its AVA-101 research in approximately 2008. *See* Lions Eye Institute, Annual Report, 10 (2014). "Following an approval from the . . . TGA – the know-how and associated data" for AVA-101 "were acquired by Avalanche . . ." Lions Eye Institute, Annual Report, 35 (2013). Thus, in March 2010, Avalanche entered into a research collaboration agreement with LEI whereby Avalanche licensed certain intellectual property rights in LEI's ophthalmology platform, including the rights to develop AVA-101. *See* Avalanche Biotechnologies, Inc., Registration Statement (Form S-1), F-22 (2015) ("**2015 Registration Statement**").

53. Shortly thereafter, Chalberg and Schwartz collaborated with Rakoczy and Dr. Ian Constable ("**Constable**"), also of LEI, to create the study design and seek regulatory approval of a multi-phase trial to test AVA-101 in human patients. *See* Ex. C, Elizabeth P. Rakoczy, et al., *Gene therapy with recombinant adeno-associated vectors for neovascular age-related macular degeneration: 1 year follow-up of a phase 1 randomised clinical trial,* 386 The Lancet 2395, 2402 (2015).

54. The AVA-101 Trial was registered with the Therapeutics Goods Administration ("**TGA**") which is Australia's analog to the U.S. Food and Drug Administration ("**FDA**"). To conduct a gene therapy trial in Australia, a sponsor must first submit the proposed trial protocol to

the applicable Human and Research Ethics Committee ("**HREC**")[3] and the National Health and Medical Research Counsel ("**NHMRC**"). *See* Therapeutic Goods Administration, *Access to Unapproved Therapeutic Goods*, 18 (2004). Once the HREC and NHMRC approve the protocol, the sponsor submits an application under the Clinical Trial Exemption Scheme to the TGA for approval. *Id*.

55. After the TGA approved the application for the AVA-101 Trial, on December 14, 2011, Avalanche filed with www.clinicaltrials.gov[4] an overview of the trial protocol ("**Trial Overview**") for its trial entitled "A Phase I/II Controlled Dose-escalating Trial to Establish the Baseline Safety and Efficacy of a Single Subretinal Injection of rAAV.sFlt-1 Into Eyes of Patients With Exudative Age-related Macular Degeneration (AMD)," identifier number NCT01494805. *See* Ex. D, Safety and Efficacy Study of rAAV.sFlt-1 in Patients With Exudative Age-Related Macular Degeneration (AMD), Clinicaltrials.gov, https://www.clinicaltrials.gov/ct2/show/NCT01494805?term=avalanche&rank=3 (last visited Jan. 25, 2016).

56. The AVA-101 Trial was arranged to take place in Australia at Sir Charles Gairdner Hospital with LEI acting as the trial investigator. Constable was the Principal Clinical Investigator and performed the subretinal injections on each patient. *See* Elizabeth Rakoczy, Lion's Eye Institute, *Application for Funding: Project Grants 2010 round – for funding 2011*, 7-8 (2010). He was also responsible for all aspects of the participants' welfare and clinical data interpretation, and supervising the collectors of clinical data and imaging. *See id.* Rakoczy was responsible for liaising with clinical, statistical, and research staff, data management and interpretation, and liaising with patients if necessary. *See id.* Dr. Chooi-May Lai ("**Lai**"), another doctor on the team at LEI, managed the data generated and interpreted the results from the trial. *See id.*

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[3] The institution where the trial will be conducted has an HREC that assesses the scientific validity of the trial design, the safety and efficacy of the medicine and the ethical acceptability of the trial process. Here, the HREC was based at Sir Charles Gairdner Hospital in Nedlands, Australia, which is the only testing site for the trial and regularly serves as LEI's patient treatment facility. *See* Ex. C, Lancet at 2397.

[4] Clinicaltrials.gov is a website established by the National Institutes of Health.

57. Avalanche and LEI were sponsors of and collaborators on the study. *See* Ex. E, Lions Eye Institute, Annual Report, 20 (2012); Ex. F, *Trial Review*, Australian New Zealand Clinical Trials Registry, https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=3404&isClinicalTrial=True (last visited Dec. 2, 2016); ECF No. 74 at 6, ECF No. 105 at 7.

58. The trial was a single-center, ***open-label study***[5] that was designed to treat patients aged 65 or above who have Wet AMD. *See* Ex. D, Trial Overview at 1; Thomas W. Chalberg, CEO, Avalanche Biotechnologies, Inc., AVA-101 Phase 2a Study Results Call, 3 (June 15, 2015) (transcript on file with Bloomberg, Inc.). Patients were sequentially randomized to receive either a dose of AVA-101 or to be assigned to the control group. *See id.* at 1. Patients in both groups were eligible to receive "rescue therapy" with ranibizumab as needed. *See* Ex. D, Trial Overview at 3.

59. The AVA-101 Trial was one study broken into two phases (Phase 1 and Phase 2a). *See id.* at 2. The AVA-101 Trial was conducted under a single trial protocol which provided for the same endpoints for both phases. *See id.* at 1; Ex. F, Trial Review ("[T]he reinjection criteria for the Phase 2a are identical to the Phase 1. And those are based on visual acuity, OCT, and fluorescein angiography. And so any increases in that activity would warrant a rescue treatment.").

60. The primary endpoint of the AVA-101 Trial—the "safety endpoint"—was to measure "ophthalmic safety" by ensuring there were no signs of unresolved ophthalmic complications, toxicity, or systemic complications as measured by laboratory tests from 1 month post injection. *See id.* at 15. "Ophthalmic safety" was to be determined by reviewing abnormal laboratory data and conducting an ocular examination of (a) ocular inflammation; (b) intraocular pressure; (c) ***visual acuity ("BCVA")***; and (d) ***retinal bleeding***.[6] *See id.* at 15. Ophthalmic safety was assessed by using biomicroscopy, indirect ophthalmoscopy, ***Spectral Domain Optical***

[5] An open-label trial is the type of trial where both the investigators and the subjects know which treatment is being administered.

[6] Retinal bleeding, or vitreous hemorrhaging, is detected through SD OCT. *See Vitreous Hemorrhage*, Retina Eye Specialists, http://www.retinaeye.com/vitreoushemorrhage.html (last visited Nov. 10, 2016).

Coherence Tomography ("SD OCT"), Color Fundus (retinal) Photography (CFP), and ***Fluorescein Angiography ("FA")***. *See* Ex. G, Elizabeth P. Rakoczy, et al., The First Report on a rAAV.sFlt-1 Phase I/II Trial for Wet Age-Related Macular Degeneration (AMD) (2012) (Discussing safety and stating, "[a]t day 60 none of the patients required rescue treatment. There was no evidence of visual acuity loss, IOP elevation, retinal detachment, or any intraocular or systemic immune response in any of the patients."); *see also* Ex. H, Elizabeth P Rakoczy, et al., One Year Follow-Up Report on the rAAV.sFlt-1 Phase I Gene Therapy Trial for Exudative Age-Related Macular Degeneration, 55 IOVS 1309 (2014) ("***Ophthalmic safety*** was assessed by biomicroscopy, IOP, indirect ophthalmoscopy, ***SD OCT***, CFP and ***FA***.") (the "**April 2014 Abstract**"); Ex. C, Lancet at 2402 ("***Ocular safety*** was monitored at each monthly visit with ***BCVA***, intraocular pressure, slit lamp biomicroscopy, indirect ophthalmoscopy, and ***SD-OCT***[.]").

61. The secondary endpoint of the AVA-101 Trial—the "efficacy endpoint"—was to determine the maintenance or improvement of vision ***without the need for ranibizumab rescue injections***. This was to be measured by (a) ***best-corrected visual acuity (BCVA)***; (b) CNV lesion (a/k/a fluid leakage), ***detected through FA***; and (c) foveal thickness (a/k/a retinal thickness), ***detected through SD-OCT***. *See* Ex. D, Trial Overview at 15. A chart displaying the two sets of endpoints is set forth below:

Primary Endpoint—Safety Measures	**Secondary Endpoint—Efficacy Measures**
visual acuity (BCVA)	visual acuity (BCVA)
Spectral Domain Optical Coherence Tomography (SD OCT)	retinal thickness detected through SD OCT
Fluorescein Angiography (FA)	CNV lesions a/k/a fluid leakage detected through FA
biomicroscopy	rescue injections
indirect ophthalmoscopy	
Color Fundus (retinal) Photography (CFP)	
ocular inflammation	
intraocular pressure (IOP)	

retinal bleeding	

62. ***Contrary to what defendants previously led the Court to believe without any basis*** (ECF No. 105 at 6), the AVA-101 Trial was ***not*** powered to show statistically significant results for efficacy. Chalberg himself explained this stating: "Our Phase 2a trial is a safety study . . . This study is not powered for statistical significance of secondary endpoints." Interview with Dr. Thomas Chalberg, CEO, and Dr. Mark Blumenkranz, Chairman of the Board, Avalanche Biopharmaceuticals, Inc., *via* e-mail (May 22, 2015), *available at* http://seekingalpha.com/article/3205796-avalanche-management-addresses-wall-streets-concerns-ahead-of-binary-catalyst. Rakoczy also stated the following: "This study was designed as a phase 1 study to assess the safety of the subretinal procedure and rAAV.sFLT-1. Hence, it was not powered to draw definitive conclusions about differences in efficacy between groups." Ex. C, Lancet at 2403.

63. During the Trial, all subjects were to receive two initial doses of ranibizumab at day 0 and week 4 and the subjects in the active arm received AVA-101 at week 1. *See* 2014 Registration Statement at 83. Beginning with the week 8 visit, ranibizumab was to be given as rescue therapy on an as-needed basis. *See id.* ***This date was chosen because after 8 weeks, the period of time was adequate for protein expression to develop from the AVA-101 injection***. Ex. C, Lancet at 2396.

64. According to Rakoczy:

> Rescue treatment with ranibizumab was given when active choroidal neovascularization progression was detected, as measured by: (1) loss of ten or more letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale from previous visit, or loss of five or more letters from previous visit on ETDRS scale in conjunction with patient perception of functional loss where such loss is attributable to choroidal neovascularisation; (2) any choroidal neovascularization related increased subsensory, intraretinal, or sub-RPE fluid on OCT; or (3) signs of increased choroidal neovascularisation leakage on FA.

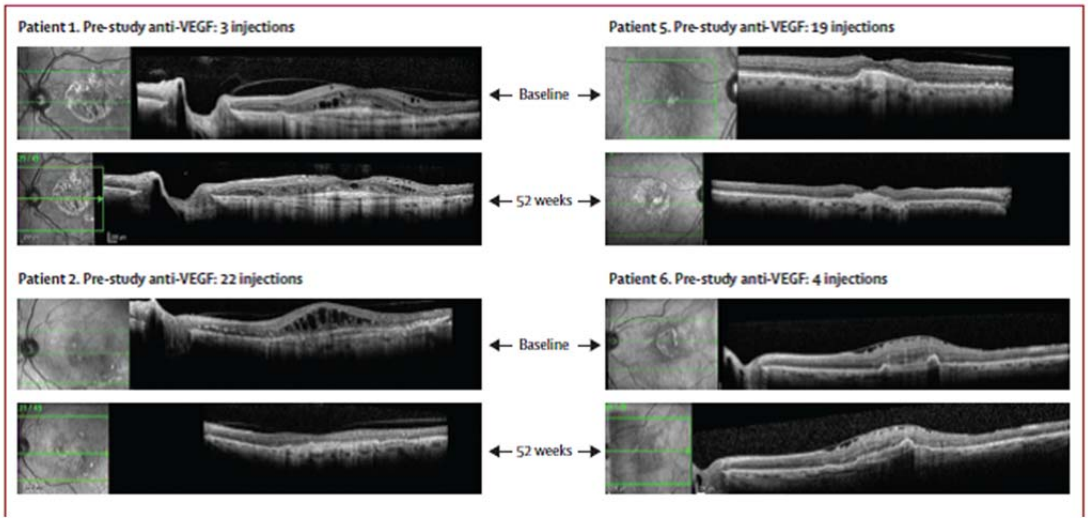
Ex. C, Lancet at 2397. In general terms, this means that rescue injections were based upon pre-specified levels of (1) worsening visual acuity, (2) increases in retinal thickness, and (3) increases

in CNV fluid leakage. *See id.* at 2398, 2399, & 2400 (Describing "[b]aseline best corrected visual acuity" by "ETDRS Letters"; discussing retinal thickness results; and describing FA assessments as showing no "recurrence of leakage"). These pre-specified criteria for rescue therapy were chosen to "assess signals of efficacy, protect patient safety, and to assess the long term treatment effect" of AVA-101. Ex. C, Lancet at 2397.

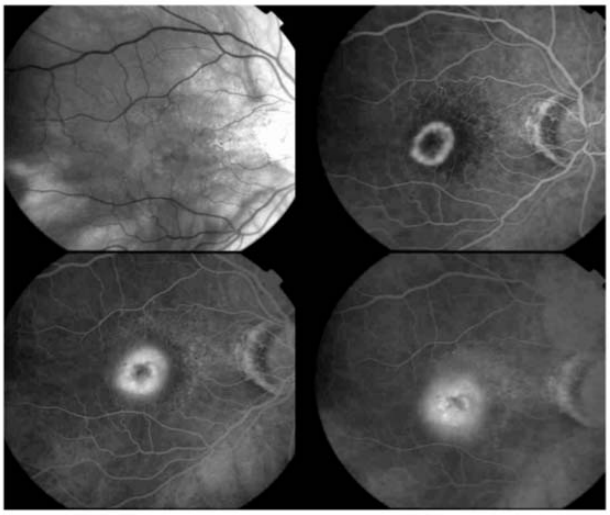
65. Visual acuity is the clearness or sharpness of vision measured at the distance of 20 feet. *See* Visual Acuity: What is 20/20 Vision?, American Optometric Association, http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/visual-acuity?sso=y (last visited Jan. 29, 2016). As explained by Rakoczy, the Early Treatment Diabetic Retinopathy Study ("**ETDRS**") scale, which is a standard eye chart characterized by rows of letters decreasing in size, was used to measure visual acuity in the AVA-101 Trial. *See* Ex. C, Lancet at 2397. An example of the ETDRS scale is included below:

66. Retinal thickness is increased when there is a buildup of fluid in the retina. The fovea is the largest concentration of cone cells in the eye located in a small pit in the center of the retina. *See* Abstract, Adaptation of the Central Retina for High Acuity Vision: Cones, the Fovea and the Avascular Zone, *available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658155/. In the AVA-101 Trial retinal thickness was measured by Spectral Domain Optical Coherence

Tomography, SD OCT, which is a non-contact medical imaging technology similar to an ultrasound or MRI that takes 3-D cross-sectional images of the retina. Zahid Yaqoob, et al., *Spectral domain optical coherence tomography: a better OCT imaging strategy*, 39 BioTechniques S6 (2005); Press Release, Avalanche Biotechnologies, Inc., *Avalanche Biotechnologies, Inc. Announces Positive Top-Line Phase 2a Results for AVA-101 in Wet Age-Related Macular Degeneration* (June 15, 2015) ("mean change from baseline in retinal thickness as measured by SD-OCT"). SD-OCT images of the retinas of several patients treated in the AVA-101 Trial are included below:



67. Fluid leakage into the retina was detected through a fluorescein angiography ("**FA**") test. *See* Ex. C, Lancet at 2400; *Fluorescein Fundamentals*, Ophthalmic Photographers' Society, http://www.opsweb.org/?page=FA (last visited Jan. 29, 2016). FA is performed by injecting a fluorescent dye into a peripheral vein. *See id.* Then, as the dye courses through and highlights the blood vessels in the eye, a specialized fundus camera or scanning laser ophthalmoscope is used to capture rapid-sequence photographs of the retina to determine the presence of blood vessel leakage. *See id.* Below are FA images of patients with Wet AMD:



68. These three measures—(1) worsening visual acuity, (2) increases in retinal thickness, and (3) increases in CNV fluid leakage—are the mostly commonly accepted measures used to determine whether a drug is inhibiting VEGF and causing an anti-VEGF response in the eye; therefore, they are not only the criteria for giving rescue injections in standard practice, they are also the three measures used to determine the secondary endpoint of efficacy. *See* Aetna No. 0701, *Vascular Enothelial Growth Factor Inhibitors for Ocular Indications*, *available at* http://www.aetna.com/cpb/medical/data/700_799/0701.html. Because rescue injections were given to patients in the AVA-101 Trial based upon pre-specified criteria for these three measures, a cursory review of the efficacy data collected would indicate how many rescue injections were given to each patient.

69. A close look at the Trial Overview and Phase 1 data makes clear that many of the critical methods for measuring these endpoints were in fact the same. "Ophthalmic safety" was to be determined by reviewing abnormal laboratory data and conducting an ocular examination of (a) ocular inflammation; (b) intraocular pressure; (c) ***visual acuity***; and (d) ***retinal bleeding***. *See* Ex. D, Trial Overview at 15. Ophthalmic safety was assessed by using biomicroscopy, indirect ophthalmoscopy, ***SD OCT***, CFP, and ***FA***. *See* ¶60. The secondary endpoint was to determine whether patients treated with AVA-101 required rescue injections by measuring (a) ***visual acuity***; (b) retinal thickness using ***SD OCT***; and (c) leakage using ***FA***. *See* ¶61. Accordingly, the "safety data" for the AVA-101 Trial, specifically, visual acuity and retinal bleeding and SD OCT and FA images, would also necessarily indicate the efficacy data because those same measures were used to

determine efficacy, *i.e.* when rescue injections were required. The following chart shows the overlap in the measurements for the primary and secondary endpoints:

Endpoint Measures	Primary—Safety	Secondary—Efficacy
Biomicroscopy	✓	
Indirect Ophthalmoscopy	✓	
Retinal Thickness (SD OCT)	✓	✓
CFP	✓	
CNV Leakage (FA)	✓	✓
Visual Acuity	✓	✓
Ocular Inflammation	✓	
Intraocular Pressure (IOP)	✓	
Retinal Bleeding	✓	
Rescue Injections[7]	✓	✓

70. The standard therapy was given on day 0 and week 4. The subretinal injection was given to the treatment arm on week 1, and beginning with week 8, study visits were to occur every 4 weeks for 52 weeks for both the treatment arm and the control arm, totaling 12 visits. *See* Ex. C, Lancet at 2396. At each visit, patients were permitted to receive rescue injections according to a prespecified criteria based on BCVA, SD-OCT, and FA. Laboratory tests were also conducted. *See id.* The chart below was submitted with the Application Background and Research Plan for the AVA-101 Trial submitted to the TGA. The chart does not include every Trial visit; however, it shows the assessments that were conducted at each Trial visit:[8]

[7] As explained in ¶68 a review of visual acuity, SD-OCT, and FA, the three measures used for the efficacy endpoint, which are also measures for the safety endpoint, would indicate the number of rescue injections required.

[8] While the source document does not provide a definition for the acronyms "SCR" and "BSL" used in the chart, counsel assumes those stand for "screening" and "baseline" assessments.

Table 1: Schedule of Assessments for AAV.sFlt-1 Injection

Procedures /Assessment	Week	SCR	BSL			1	2	4	8	12	16	24or early exit	36	52/ 78/ 156
	Visit	1	2	3	4	5	6	7	8	9	10	11	12	13
	day	-14 to -1	1	+1 day	+4 days	+7 days	14	30	60	90	120	180	210	360
Informed Consent , inclusion/exclusion criteria		X												
Medical /ophthalmic history		X												
Demography[1]		X												
Physical Examination		X												
Vital Signs (temperature, blood pressure & pulse rate)		X	X	X	X	X	X	X	X	X	X	X	X	X
ECG		X				X			X			X		X
BCVA by ETDRS		X	X		X	X	X	X	X	X	X	X	X	X
Biomicroscopic examination		X[2]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]	X[2]
IOP		X[2]	X	X[3]	X[3]	X[3]	X[3]	X	X	X	X	X[2]	X[2]	X[2]
Indirect ophthalmic examination		X[2]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]	X[2]
OCT		X[2]	X[3]					X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]
Colour fundus photos		X[2]						X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]
Fluorescein Angiogram		X[3]						X[3]	X[3]	X[3]		X[3]	X[2]	X[2]
Laboratory tests[4]		X		X	X	X	X	X		X		X	X	X
Urinalysis		X		X	X			X		X		X	X	X
Therapeutic Drug Monitoring – PK[5]		X		X			X	X	X	X	X	X	X	X
Anti-VEGF ITV Injection[5]			X					X	(X)	(X)	(X)	(X)	(X)	(X)
Hospital Admission			X											
AAV.sFlt-1 Injection			X											
Concomitant medications		X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events[6]			X	X	X	X	X	X	X	X	X	X	X	X

AE = Adverse event; ECG = Electrocardiogram; BCVA = Best Corrected Visual Acuity; ETDRS = Early treatment diabetic retinopathy study; IOP = Intraocular pressure; OCT= Optical coherence tomography. Visit schedules may deviate.

1. Height and weight should be measured at the screening visit
2. Assessment performed in both eyes
3. Assessment performed in study eye only
4. Laboratory tests include: haematology (haemoglobin, platelets, WBC & differential); renal function (serum and blood urea nitrogen); hepatic function (serum bilirubin, alkaline phosphatase, GGT, SGOT/AST and SGPT/ALT); electrolytes (sodium, potassium, chloride, bicarbonate, calcium, phosphate). T-cell response will also be monitored. **At these time points tears, blood, urine and saliva samples will also be collected and analysed for AAV.sFlt-1 by real-time PCR, for presence of AAV capsid by ELISA and for changes in sFlt-1protein concentration by ELISA as proposed in this application.*
5. (X) means treatment provided only if required
6. AEs, after the first administration of study drug, should be recorded from the time of signing the informed consent form until the patient completes the study. If a subject withdraws, AE should be recorded until withdrawal or 30 days after the last dose of study drug, whichever is later.

71. The Trial Overview provides that the AVA-101 Trial primary safety endpoint data for the AVA-101 Trial would be reviewed one month after injection and at additional intervals thereafter during the extended follow-up period. *See* Ex. D, Trial Overview at 2-3. The patients

would remain on-study for 52 weeks, at which point the top-line data would be reviewed. *See* Ex. H, April 2014 Abstract. Then, after that period of time, the Company would schedule two follow-ups at 18 months and 36-months after the first injection at which time the safety analysis for the primary endpoint was conducted. *See* Samuel B. Barone, CMO, Avalanche Biotechnologies, Inc., AVA-101 Phase 2a Study Results Call, 3 (June 15, 2015) (transcript on file with Bloomberg, Inc.).

C. Safety Monitoring for Phase 1 and Phase 2a of the AVA-101 Trial

72. When conducting a clinical trial, the TGA provides that "[t]he sponsor is responsible for the ongoing safety evaluation of the investigational product(s)" and must conduct an "ongoing review and analysis of all information that is pertinent to the safety or benefit-risk assessment of the product." *See* Therapeutic Goods Administration, *Note for Guidance on Good Clinical Practice*, §5.16.1 (2000) ("**TGA GCP Guide**"); Therapeutic Goods Administration, *Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines*, §2.3.2 (2014) ("**TGA Pharmacovigilance Requirements**"). The FDA requires that "[t]he sponsor must promptly review all information relevant to the safety of the drug obtained or otherwise received by the sponsor from foreign or domestic sources" (21 C.F.R. § 312.32(b)) and "[t]he sponsor shall review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator (21 C.F.R. § 312.56(c)).[9]

73. "Safety analysis entails continuous surveillance of many variables with many subclassifications in the effort to look for signals of risk." Jay Herson, Data and Safety Monitoring Committees in Clinical Trials 48 (Shein-Chung Chow et al. eds. 2009). "Adequate surveillance requires integration of safety data from multiple sources, across multiple trials and even multiple indications during clinical development in order to characterize the developing safety profile." Laura McKain, M.D. et al., *Optimizing Safety Surveillance During Clinical Trials Using Data Visualization Tools*, Drug Discovery & Development (Oct. 6, 2015, 10:23 AM),

[9] While the AVA-101 Trial was registered with the TGA and thus subject to Australian regulations, Avalanche intended to seek approval of AVA-101 from the FDA, thus testing of the drug must likewise have complied with FDA regulations. *See* 2014 Form 10-K at 25.

http://www.dddmag.com/article/2015/10/optimizingsafetysurveillanceduringclinicaltrialsusingdatavisualizationtools ("Pharmaceutical companies must continuously monitor the safety of investigational products in development for adverse events that may be unexpected, occur at an increased frequency or severity, or result in an unexpected outcome. Ongoing safety signal detection leads to optimal patient protection and is essential to obtaining regulatory approval.") ("**Safety Surveillance Article**"). Thus, the FDA dictates that a sponsor should set up a systematic approach for safety surveillance that includes "a process for reviewing, evaluating, and managing accumulating safety data from the entire clinical trial database at appropriate intervals." *See* U.S. Food and Drug Administration, Guidance for Industry and Investigators: Safety Reporting Requirements for INDS and BA/BE Studies, at 13 (2012) ("**FDA Safety Reporting Guide**"). This requires establishing a central safety database where the safety data can be compiled and organized for review. *See* Safety Surveillance Article at 2.

74. During the course of conducting safety surveillance, the TGA provides that "[t]he sponsor should promptly notify all concerned investigator(s)/institution(s) and the regulatory authority(ies) of findings that could affect adversely the safety of the subjects, impact the conduct of the trial, or alter the IRB/IEC's approval/favourable opinion to continue the trial." TGA GCP Guidance, §5.16.2.

75. Thus, all of the safety assessments indicated in the chart in ¶70 *supra* recorded at each patient visit would have been compiled and analyzed on an ongoing basis for safety signals and risks as part of the trial's safety surveillance program. Constable was responsible for overseeing the collection of the data; Rakoczy and Lai were responsible for managing the data that had been generated. *See* ¶¶51, 56, 60.

76. A data-monitoring committee ("**DMC**") "may be established by the sponsor to" review the accumulating safety surveillance data and "assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial." TGA GCP Guide §1.25. "In some cases, a specific independent committee with substantial external representation could be created to perform this

function. In others, the sponsor may choose to create a safety team within the sponsor's organization." FDA Safety Reporting Guide at 13. "In either case, this independent group would oversee the evolving safety profile of the investigational drug and evaluate, at appropriate intervals, the accumulating data from individual and multiple clinical trials, as well as other available information." *Id.*

77. "A fundamental reason to establish a DMC is to enhance the safety of trial participants in situations in which safety concerns may be unusually high, in order that regular interim analyses of the accumulating data are performed." U.S. Food and Drug Administration, Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees, §2.1 (2006) ("**FDA DMC Guidance**"). The FDA recommends assembling a DMC in certain circumstances, including when "[t]here are *a priori* reasons for a particular safety concern, as, for example, if the procedure for administering the treatment is particularly invasive[.]" *Id.*

78. In order to evaluate the accumulating data in the trial, "[t]he study protocol will generally describe the schedule of interim analyses to be considered by the DMC, or the considerations that will determine the timing of meetings (e.g., a plan for interim analysis after a certain number of primary outcomes have been reported)." *Id.* at §4.3.1.1. An interim analysis reviews all of the safety and/or efficacy data accrued to date in order to compare treatment arms. *See* International Conference on Harmonization (ICH) guidance, E9 Statistical Principles for Clinical Trials, §4.5 (1998) ("**ICH E9 Guidance**") (Interim analysis "is any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to formal completion of the trial[.]").[10] Thus, "[i]nterim analysis requires unblinded . . . access to treatment group assignment (actual treatment assignment or identification of group assignment) and comparative

[10] Both the FDA and the TGA have adopted these ICH guidelines. *See E9 Statistical Principles for Clinical Trials*, ICH, http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/statistical-principles-for-clinical-trials.html (last visited Nov. 16, 2016); *Clinical and Safety Guidelines*, TGA, https://www.tga.gov.au/clinical-efficacy-and-safety-guidelines (last visited Nov. 16, 2016).

treatment group summary information." *Id.* "The study protocol will also typically describe the statistical approach to the interim analysis of trial data." FDA DMC Guidance §4.3.1.1.

79. In conducting the interim analysis, DMC usually receives an "interim report . . . that includes comparative effectiveness and safety data presented by study group[.]" *Id.* at §4.2.2. While the interim reports are often only reviewed by the DMC, "[i]n some cases (for example, ***in open-label trials with special concerns about safety***), there may be a rationale for the sponsor and/or investigators to have access to the ongoing comparative safety data to ensure continuous monitoring[.]" *Id.* at §4.2.2. As well, "the review of interim comparative data may raise certain questions that the DMC might want to address to the sponsor. These interactions may improve the quality of the monitoring process and may also provide the sponsor with information relevant to the costs, timetable, and likely interpretability of the study that can be of significant value in planning future studies and/or other aspects of product development." *Id.* at §6.2; ICH E9 Guidance at §4.5 ("[I]t is recognised that drug development plans involve the need for sponsor access to comparative treatment data for a variety of reasons, such as planning other trials.").

80. Another "fundamental responsibility of a DMC is to make recommendations to the sponsor . . . concerning the continuation of the study. Most frequently, a DMC's recommendation after an interim review is for the study to continue as designed." *Id.* at §4.4.3.1. "Other recommendations that might be made include study termination, study continuation with major or minor modifications, or temporary suspension of enrollment and/or study intervention until some uncertainty is resolved." *Id.*

81. For the AVA-101 Trial "[s]tudy data ***and*** adverse events were monitored by a data safety monitoring committee with expertise in retinal diseases and gene therapy vectors." Ex. C, Lancet at 2398. The DMC reviewed interim safety surveillance data in June 2014. *See* 2014 Form 10-K at 1. Indeed, Avalanche explained to an analyst that "[t]he trial included an interim safety analysis which was conducted in June of 2014" which revealed no issues. Phil Nadeau, Cowen & Co., *Highlights from Lunch with Management*, 1 (2015); *see also* Joshua Schimmer, Piper Jaffray, *Avalanche Biotechnologies (AAVL), On the Road With Management; Increasing PT*, 1 (2014) (after

hosting Avalanche for meetings stated the report "AAVL remains on track to report topline data in the middle of 2015, following a prior interim safety look that revealed no safety concerns.").

D. Progression of Phase 1 and Phase 2a of the AVA-101 Trial

82. Phase 1 of the AVA-101 Trial began in January 2012, and by April 2012 all 8 patients had been enrolled. Pursuant to the Trial Overview, the one-month primary endpoint (safety) data for the 8 patients was gathered. *See* Ex. D, Trial Overview at 2-3. Furthermore, an additional 8-week safety evaluation was conducted for Phase 1. The results of this 8-week evaluation were reported at the meeting of the American Society for Cell and Gene Therapy held in May 2012. *See* Ex. E, 2012 LEI Annual Report at 20; Ex. C, Lancet at 2396. The meeting abstract published on May 3, 2012 stated that "***[a]t day 60 none of the patients required rescue treatment***. ***There was no evidence of visual acuity loss***, IOP elevation,[11] ***retinal detachment***,[12] or any intraocular or systemic immune response in any of the patients." Ex. G, May 2012 Abstract. This abstract indicates that the safety/efficacy endpoint measures were evaluated at week 8. ***Rakoczy explained that this 8-week marker was significant as "this period of time provided an adequate window to allow time for the start of sFLT-1 protein expression" to develop from the AVA-101 injection***. Ex. C, Lancet at 2396. Indeed, the fact that the 8-week data was announced to the medical community demonstrates that beyond a doubt 8-week data was material.

83. Beginning in April 2012 Avalanche began enrolling patients in Phase 2a of the AVA-101 Trial. *See* 2014 Registration Statement at 2.

84. By the end of 2012, 12 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Ex. E, LEI 2012 Annual Report at 20. And by the end of 2013, 30 patients had been enrolled in Phase 2a. *See* Lions Eye Institute, Annual Report, 31, 35 (2013).

85. Prior to February 8, 2014, all 32 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Ex. J, Ocular Gene Therapy Showed Fewer Injections Needed, Increased Visual

[11] "**IOP**" is an acronym for intraocular pressure.

[12] Retinal detachment is detected through SD OCT.

Gain, Retina Today (2014), http://retinatoday.com/2014/04/ocular-gene-therapy-showed-fewer-injections-needed-increased-visual-gain.

86. In or around April 2014, LEI and the Company began to publicize the remarkable 52-week results from the first 8 patients enrolled in Phase 1 of the AVA-101 Trial. Specifically, the results showed that in Phase 1, AVA-101 had the desired effect in the treatment arm as on average retinal thickness ***decreased by 200 um***, ***visual acuity increased by 7.5 letters***, and 5 of 6 patients in the treatment arm did not receive any rescue injections, meaning that out of a possible 72 rescue injections, ***only 2 rescue injections were given (both to the same patient)***. Control subjects received ten times more rescue injections than patients in the treatment arm. *See* Ex. H, April 2014 Abstract; Ex. I, Elizabeth P. Rakoczy, et al., *Gene Therapy for Wet-AMD: Progress Report on Phase I/II Clinical Trial*, 21 Molecular Therapy S22 (2013). These results provided hope that one subretinal injection of AVA-101 might cure Wet AMD because nearly every patient was able to maintain stable vision without the need for a rescue injection for an entire year. As one analyst noted, "the proof-of-concept results are impressive ***with a functional cure*** in patients" treated in Phase 1 of the AVA-101 Trial. Tim Lugo, William Blair, *ARVO Wrap-Up: Gene Therapies Continue to Look Impressive Ahead of 2015 Data Sets*, 2 (2015).

E. The IPO and the 2015 Offering

87. On May 30, 2014, Avalanche launched its Initial Public Offering ("**IPO**") by filing a registration statement with the SEC on Form S-1 (Registration No. 333-197133). Following amendment, on July 30, 2014 the SEC declared the registration statement effective. The Securities Act Defendants priced the IPO at $17 per share. On July 31, 2014, Avalanche and the Individual Securities Act Defendants filed the final prospectus for the IPO (the "**2014 Prospectus**"), which forms part of the registration statement (the 2014 Prospectus and registration statement are collectively referred to herein as the "**2014 Registration Statement**"), and sold 6,900,000 shares of common stock to the investing public. The IPO was completed on August 5, 2014 and Avalanche raised $106.8 million, after deducting underwriting discounts and commissions and estimated

offering expenses. *See* Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (Aug. 5, 2014).

F. The Phase 2a Topline Results

88. On June 15, 2015, Avalanche released the top-line results from Phase 2a of the AVA-101 Trial. The results indicated that AVA-101 ***was not effective*** in treating patients with Wet AMD, nor was it a one-time cure for the disease. Avalanche Biotechnologies, Inc., Quarterly Report (Form 10-Q), 17 (Nov. 9, 2015) (stating that AVA-101 "did not [show] evidence of a complete and/or durable anti-VEGF response in the majority of subjects treated with AVA-101 as administered in the Phase 2a study."). While the "study met its 12-month primary endpoint, demonstrating that AVA-101 was well tolerated with a favorable safety profile in subjects with wet AMD. No serious adverse events related to AVA-101 were observed[;]" retinal thickness, a critical anatomic efficacy measure, ***increased in patients treated with AVA-101 by 25 microns*** whereas it decreased in the control group by 56 microns. *Id.* at 15. This means that AVA-101 was not only ineffective at inhibiting blood vessel growth and leakage in the retina, it fell far behind the current therapy. As a gene therapy, AVA-101 was designed to permanently change the cells in the retina to combat VEGF, eliminating the need for another injection over the patient's lifetime. However, the results from the Trial showed that AVA-101-treated subjects received "***a mean of 3.1 rescue injections***" compared with "***a mean of 3.6 rescue injections*** for subjects in the control group." This near equivalent mean measurement occurred because 10 of the 21 patients who were treated with AVA-101 received ***between 3 and 7 rescue injections***, whereas 10 of the 11 patients treated in the control group needed ***between 3 and 5 rescue injections***. *See id.* Clearly the drug did not work as intended, and for some patients was less effective than the current therapy. Finally, the improvement in ***visual acuity was an improvement of only 2 letters*** which was negligible. These results stand in stark contrast to the Phase 1 results showing a ***decrease in retinal thickness by 200 um***, an ***increase in visual acuity by 7.5 letters***, and ***5 of 6 patients needing 0 rescue injections***.

89. At the time of the IPO in July 2014, a sufficient amount of the aforementioned negative safety/efficacy data existed to indicate that AVA-101 was not having the desired effect in

patients enrolled in Phase 2a. In any event, the existing data materially undermined the likelihood that AVA-101 was effective.

90. First, consistent with the Trial Overview and the analyses conducted in Phase 1 of the Trial, interim safety/efficacy endpoint analyses were conducted at week 4 and week 8 (and likely at additional times thereafter) for all patients enrolled in Phase 2a of the Trial. *See* ¶¶55, 63, 69-71, 82. Because the Trial was fully enrolled by February 8, 2014, by July 2014, each patient in Phase 2a was already well past week 8 of treatment and its corresponding interim analysis. Avalanche admitted that within the first 8 weeks of treating patients in Phase 2a, data showed that retinas were thickening for patients in the treatment arm and thinning for patients in the control arm by a difference of 81 um—the opposite of what you would see with an effective drug—and this delta remained constant throughout the Trial. *See* Salveen Richter, SunTrust Robinson Humphrey, *Await Further AVA-101 Clarity, Lack of Near-Term Catalysts, DGrading to Neutral*, 1 (2015). Thus, the trend of retinas thickening in the treatment group and thinning in the control group would have been visible in the safety data for all patients at least by the interim 8-week analyses that were performed and certainly by the date of the IPO given the timing of patient enrollment described above.

91. Next, by the end of 2012, 12 patients had been enrolled in Phase 2a of the AVA-101 Trial, meaning that the full 1-year data was available for the first 12 of 32 patients by December 2013. *See* Ex. E, LEI 2012 Annual Report at 20. By the end of 2013, 30 of 32 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Lions Eye Institute, Annual Report, 31, 35 (2013). If patients enrolled steadily throughout the year of 2013, the full 1-year data would have most likely been available for 22 of 32 patients by July 2014,[13] and 7-month or longer data would have been available for the remaining 8 patients enrolled in the latter half of 2013. Even in the highly unlikely event that all 18 additional patients enrolled at the last possible moment in December 2013, the July

[13] The 22 patient tally was calculated by adding the 12 patients enrolled in 2012 to 10 patients, or the number of additional patients enrolled by July 2013 if 1.5 patients enrolled per month in 2013.

2014 data would represent 1-year data for 12 patients, 7-month data for 18 patients, and at least 5-month data for the 2 patients who enrolled in 2014. *See* Ex. J, Retina Today Article. This data would have been sufficient to indicate that retinas were thickening in the treatment group and that patients in the treatment group were receiving rescue injections at a materially higher rate than those in Phase 1 of the AVA-101 Trial.

G. Events After Announcement of the Phase 2a Results

92. When the Phase 2a results were announced, it was obvious to the market that the trial was not effective as Avalanche common stock dropped $21.83, or more than 56%, to close on June 16, 2015 at $17.05 per share.

93. On June 16, 2015, in an article entitled "Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club," one commentator stated that "I'm struggling to adequately describe the awfulness of Avalanche Biotechnologies' [] performance Monday night[.]" The author pointed out that when investors looked deeper at the results, they realized the flaws, concluding that "the painful lesson here is that Avalanche's study of AVA-101 may have achieved its primary efficacy endpoint, but the gene therapy failed the more important common sense endpoint." Adam Feuerstein, *Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club*, The Street (June 16, 2015), http://www.thestreet.com/story/13187351/1/avalanchefailscommonsensetestkickedoutofgenetherapycredibilityclub.html. Zacks called the data "lackluster" and "weak," explaining that "results disappointed investors[.]" *Avalanche Biotechnologies Slips on Weak AVA-101 Data*, Zacks Equity Research (June 16, 2015), http://www.zacks.com/stock/news/178460/avalanche-biotechnologies-slips-on-weak-ava101-data. An article published on investing website, the Motley Fool, explained that "***[t]he problem is that the retinas of patients receiving AVA-101 thickened relative to those in the control group***, casting doubt on the gene therapy's efficacy as a treatment for wet AMD[,]" "one would expect the *exact* opposite result if AVA-101 was truly helping patients maintain their visual acuity." George Budwell, *Why Avalanche Biotechnologies, Inc. Stock Collapsed Today*,

Motley Fool (June 16, 2015), http://www.fool.com/investing/general/2015/06/16/why-avalanche-biotechnologies-inc-stock-collapsed.aspx.

94. Also on June 16, 2015, William Blair downgraded Avalanche and moved its price target down to $24.00 from $53.00. *See* Tim Lugo, William Blair, *Lucentis Performance and Difficult Population Clouds Phase IIa; Phase IIb a Ways Away; Downgrading to Market Perform* (2015). SunTrust Robinson Humphrey also downgraded Avalanche and moved its price target down to $25.00 from $60.00. *See* Salveen Richter, SunTrust Robinson Humphrey, *Await Further AVA-101 Clarity, Lack of Near-Term Catalysts, DGrading to Neutral* (2015).

95. Less than two months later, the Company announced that it had decided to abandon further development of its AVA-101 Trial program for Wet AMD because the drug did not have the desired effect in patients in Phase 2a of the AVA-101 Trial. Specifically the Company stated:

> ***Overall, we did not observe evidence of a complete and/or durable anti-VEGF response in the majority of subjects treated with AVA-101 as administered in the Phase 2a study. We are continuing to analyze the Phase 2a data in order to enhance our understanding of the study results with respect to the secondary endpoints and why we did not see a more complete, durable anti-VEGF response***. To that end, we have decided not to move forward with the Phase 2b clinical trial for AVA-101 with the current dose and administration procedure that we had planned to initiate in the second half of 2015.

96. The decision to cease development based upon the poor efficacy results from Phase 2a is significant given that ***neither phase of the AVA-101 Trial was powered to demonstrate statistical significance as to efficacy***. Thus, the preliminary, un-blinded efficacy results were so obviously negative that further development was not justified.

III. ACTIONABLE STATEMENTS

97. On or about May 30, 2014, Avalanche filed with the SEC its registration statement on Form S-1 (Registration No 333-197133). Following amendment, on July 30, 2014 the registration statement was declared effective by the SEC and the Securities Act Defendants priced the IPO at $17 per share. On July 31, 2014 Avalanche and the Individual Securities Act Defendants filed the 2014 Prospectus, which forms part of the 2014 Registration Statement with the SEC, and sold 6,900,000 shares of common stock to the investing public for total proceeds of $106.8 million,

after deducting underwriting discounts, commissions, and expenses. All of the Individual Securities Act Defendants signed the 2014 Registration Statement. The IPO was completed on August 5, 2014.

98. As described below, the 2014 Registration Statement contained untrue statements of material facts or omitted to state other facts necessary to make the statements therein not misleading, and was not prepared in accordance with the rules and regulations regarding is preparation.

99. Specifically, in regard to the risks facing the Company at the time of the offering, Avalanche and the Individual Securities Act Defendants stated in the 2014 Registration Statement:

> ***Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.***
>
> * * *
>
> ***Successful continued development and ultimate regulatory approval of AVA-101 is critical for our future business success***. . . .
>
> ***The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:***
>
> ***we may not be able to provide evidence of efficacy and safety for AVA-101***;
>
> ***the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;***
>
> * * *
>
> ***Our ability to commercialize our product candidates effectively will depend on several factors, including the following:***
>
> ***successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates***
>
> * * *
>
> ***[S]uccess in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing.***
>
> * * *

> ***If our proprietary vectors are not shown to be safe and effective in targeting retinal tissue, we may not realize the value of our investment in directed evolution technology***.
>
> * * *
>
> In addition, ***success in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. . . .***
>
> ***We cannot be certain that any of our planned clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.***
>
> * * *
>
> ***The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:***
>
> ***we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication***;
>
> ***the results of clinical trials may not demonstrate the safety or efficacy required*** by such authorities for approval;
>
> * * *
>
> ***The degree of market acceptance of our product candidates will depend on a number of factors, including:***
>
> ***demonstration of clinical efficacy and safety compared to other more-established products;***
>
> * * *
>
> ***Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate is:***
>
> ***safe, effective and medically necessary***;
>
> * * *
>
> ***All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities.***

100. The foregoing statements in ¶99 were materially misleading because they omitted the following adverse facts that existed at the time of each statement and which evidenced that AVA-101 was ineffective in treating Wet AMD:

a) As explained in ¶¶48, 49, 58-61, 63-71, 81, 82, 86, 88-96, by the time of the IPO, the patients in the treatment arm were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶48, 49, 58-61, 63-71, 81, 82, 86, 88-96, by the time of the IPO, many patients in the treatment arm of Phase 2a were requiring multiple rescue injections.

101. Pursuant to Item 303(a) of Regulation S-K [17 C.F.R. § 229.303(a)] issuers are required to disclose events or uncertainties, including any known trends, that have had or are reasonably likely to cause the registrant's financial information not to be indicative of future operating results. At the time of the IPO, Avalanche and the Individual Securities Act Defendants knew that the patients in the treatment arm of Phase 2a of the AVA-101 were experiencing significant thickening—not thinning—of the retinas and were requiring multiple rescue injections. The Offering Documents, however, omitted this information. The adverse events and uncertainties associated with these negative trends were reasonably likely to have a material impact on the Company's profitability and were therefore required to be disclosed in the 2014 Registration Statement.

102. Under Item 503 of Regulation S-K, an issuer must include in its registration statement "the most significant factors that make the offering speculative or risky" and must "[e]xplain how the risk affects the issuer or the securities being offered." 17 C.F.R. §229.503. Thus, the 2014 Registration was required to include a discussion of the most significant risk facing Avalanche—that at the time of the IPO (a) patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening of the retina; (b) patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections.

103. The 2014 Registration Statement also violated Item 408 of Regulation C. Item 408 imposes a duty to disclose material information necessary to ensure that representations in a registration statement are not misleading by requiring that, "[i]n addition to the information expressly required to be included in a registration statement, there shall be added such further material information, if any, as may be necessary to make the required statements, in light of the

circumstances under which they are made, not misleading." 17 C.F.R. § 230.408(a). The 2014 Registration Statement omitted material information that was required to be disclosed to make the statements in the 2014 Registration Statement not misleading. Specifically, the statements in ¶99 were misleading in light of the Securities Act Defendants' failure to disclose that at the time of the IPO, (a) the patients in the treatment arm were experiencing significant thickening—not thinning—of the retinas; (b) many patients in the treatment arm of Phase 2a were requiring multiple rescue injections.

104. On July 30, 2014, Avalanche priced its IPO at $17.00 per share. Avalanche's stock price closed at $27.99 on the day of the IPO, climbing nearly 40% in one day, even after being priced above expectations.

105. However, to summarize the above allegations, the following conditions would have indicated that there was sufficient data existing at the time of the IPO to show that AVA-101 was not effective in treating Wet AMD and at the very least materially undermined the likelihood that AVA-101 effectively treated Wet AMD:

a) Subretinal injections are more difficult to administer and are significantly more invasive and dangerous than intravitreal injections, requiring meaningfully better efficacy to be competitive (¶49);

b) AVA-101 was designed to be a one-time, functional cure for Wet AMD, eliminating the need for rescue injections every 4 to 8 weeks (¶¶48, 50);

c) Data from Phase 1 of the AVA-101 Trial remarkably showed that over the course of an entire year, 5 of 6 patients received 0 rescue injections (¶86) and retinal thickness decreased by an average of 200 um;

d) Phase 2a of the AVA-101 Trial was open-label, meaning that data was not blinded to the parties participating in the Trial (¶58);

e) Pursuant to TGA and FDA regulations, and the AVA-101 Trial protocol, the safety/efficacy endpoint data for Phase 2a of the Trial was being continuously gathered, compiled, and managed by Constable, Rakoczy,

and Lai and intermittently reviewed by the appointed DMC (¶¶53-56, 72-81);

f) Phase 2a of the AVA-101 Trial was fully enrolled by February 8, 2014 (¶¶70, 82-86);

g) A 4 week review and 8 month review of the safety/efficacy endpoint data would have been available for all patients enrolled in the Phase 2a Trial by July 2014 (¶¶90-91);

h) Within the first 8 weeks of treating patients in Phase 2a, data showed that retinas were thickening for patients in the treatment arm and thinning for patients in the control arm by a difference of 81 um and this delta remained constant throughout the Trial. 8 week data was available for all patients by July 2014 (¶90);

i) In June 2014, the DMC reviewed safety surveillance data (¶81); and

j) The full 1-year data would have most likely been available for 22 of 32 patients by July 2014, 7-month or greater data would have been available for the remaining 8 patients who enrolled in the latter half of 2013, and 5-month or greater data would have been available for the 2 patients who enrolled in 2014. (¶91).

IV. CLAIMS FOR RELIEF UNDER THE SECURITIES ACT

COUNT I

For Violations of Section 11 of the Securities Act Against The Securities Act Defendants

106. The Securities Act Plaintiff repeats and realleges each Securities Act allegation in paragraphs ¶¶13-105 above as if fully set forth herein. This Count does not sound in fraud. Any allegations of fraud or fraudulent conduct and/or motive are specifically excluded. For purposes of asserting this and other claims under the Securities Act, the Securities Act Plaintiff does not allege that the Securities Act Defendants acted with intentional, reckless or otherwise fraudulent intent.

107. This Count is asserted against the Securities Act Defendants for violations of Section 11 of the Securities Act (15 U.S.C. § 77k), on behalf of all Securities Act Class members who purchased the Avalanche common stock sold in or traceable to the Avalanche IPO. The 2014 Registration Statement contained misrepresentations of material facts and omitted to state material facts required to be stated in order to make the statements contained therein not misleading.

108. Liability under this Count is predicated on the Securities Act Defendants' participation in the IPO.

109. As the issuer of the registered securities, Avalanche is strictly liable for the misleading statements and omission of material described herein.

110. None of the other Securities Act Defendants made a reasonable investigation or possessed reasonable grounds for the belief that the statements contained in the 2014 Registration Statement were true or that there was no omission of material facts necessary to make the statements made therein not misleading.

111. The Securities Act Defendants, issued, caused to be issued, and participated in the issuance of materially false and misleading statements to the investing public that were contained in the 2014 Registration Statement, and that misrepresented and/or failed to disclose, inter alia, the facts set forth above.

112. This action was brought within one year after the discovery of the untruthfulness of the statements and omissions or after such discovery should have been made by the exercise of reasonable diligence and within three years after Avalanche common stock was offered to the public.

113. Class members who purchased or otherwise acquired Avalanche common stock pursuant to traceable to the IPO did not know, nor in the exercise of reasonable diligence could they have known, that the 2014 Registration Statement contained untrue statements of material fact and omitted to state material facts required to be stated or necessary to make the statements particularized above not misleading when they purchased the registered securities.

114. As a result of the foregoing, the defendants named in this Count are liable for violations of Section 11 of the Securities Act.

COUNT II
For Violations of Section 15 of the Securities Act Against the Individual Securities Act Defendants

115. The Securities Act Plaintiff repeats and realleges each Securities Act allegation in paragraphs ¶¶13-114 above as if fully set forth herein. This Count does not sound in fraud. Any allegations of fraud or fraudulent conduct and/or motive are specifically excluded. For purposes of asserting this and other claims under the Securities Act, the Securities Act Plaintiff does not allege that the Securities Act Defendants acted with intentional, reckless or otherwise fraudulent intent.

116. This Count is alleged against the Individual Securities Act Defendants for violations of Section 15 of the Securities Act (15 U.S.C. § 77o), on behalf of the Securities Act Plaintiff and the other Securities Act Class members who purchased Avalanche common stock sold in or traceable to the Avalanche IPO.

117. As set forth in Count I herein, Avalanche is liable pursuant to Section 11 of the Securities Act. At all relevant times, the Individual Securities Act Defendants were controlling persons of Avalanche within the meaning of Section 15 of the Securities Act. The Individual Securities Act Defendants served as executive officers and/or directors of Avalanche prior to and at the time of the IPO as alleged herein.

118. Each of the Individual Securities Act Defendants was a participant in the violations of Section 11 of the Securities Act alleged in Count I above, based on their having signed the 2014 Registration Statement and having otherwise participated in the process that allowed the IPO to be executed. The Individual Securities Act Defendants, by virtue of their managerial and/or board positions with the Company, controlled the Company, as well as the content of the 2014 Registration Statement, at the time of the IPO. Each of the Individual Securities Act Defendants was provided with or had unlimited access to the 2014 Registration Statement, and had the ability to prevent its issuance or cause it to be corrected.

119. This action was brought within one year after the discovery of the untruthfulness of the statements and omissions or after such discovery should have been made by the exercise of reasonable diligence and within three years after Avalanche common stock was offered to the public.

120. As a result of the foregoing, the Individual Securities Act Defendants are liable under Section 15 of the Securities Act, to the same extent that Avalanche is liable under Section 11 of the Securities Act.

V. PRAYER FOR RELIEF

WHEREFORE, the Securities Act Plaintiff on behalf of himself and the Class, prays for relief and judgment including:

A. Determining that Counts I through II of this action are a proper class action under Federal Rules of Civil Procedure 23, certifying the Securities Act Plaintiff as Class representative under Rule 23 of the Federal Rules of Civil Procedure, and certifying the Securities Act Plaintiff's counsel as Class Counsel;

B. Awarding compensatory damages in favor of the Securities Act Plaintiff and the other relevant Class members against all of the Securities Act Defendants, jointly and severally, for all damages sustained as a result of the Securities Act Defendants' wrongdoing, in an amount to be determined at trial, including pre-judgment and post-judgment interest, as allowed by law;

C. Awarding rescissory damages in favor of the Securities Act Plaintiff and the other relevant Class members where appropriate against all of the Securities Act Defendants, jointly and severally, for all injuries sustained as a result of the Securities Act Defendants' wrongdoing, in an amount to be determined at trial, including pre-judgment and post-judgment interest, as allowed by law;

D. Awarding extraordinary, equitable, and/or injunctive relief as permitted by law (including, but not limited to, rescission);

E. Awarding the Securities Act Plaintiff and the Class their costs and expenses incurred in this action, including reasonable counsel fees and expert fees; and

F. Awarding such other and further relief as may be just and proper.

EXCHANGE ACT CLAIMS

121. At the beginning of 2012, with the help of its Australian trial investigator, the Lion's Eye Institute ("**LEI**"), Avalanche embarked on a clinical trial program to test its novel gene therapy, AVA-101, in patients with Wet AMD. While the current standard of care for Wet AMD required injections into the eye every 4 to 8 weeks in order to maintain stable vision, AVA-101 was designed to be a one-time genetic cure for the disease. However, in order to function properly, AVA-101 had to be administered through an invasive sub-retinal injection which was significantly more invasive than administration of the standard therapies, requiring an operation and anesthesia, and thus was subject to far more complications than the intravitreal injection of the standard therapies. In order for AVA-101 to be a worthwhile treatment for Wet AMD and to justify the risks of the more invasive procedure, AVA-101 needed to be significantly more effective than the current treatments.

122. The clinical trial of AVA-101 in patients with Wet AMD (the "**AVA-101 Trial**" or the "**Trial**") was governed by a single protocol but was broken into two phases. The Trial was open-label, meaning that the results were not blinded to the parties involved, and its primary endpoint was ocular safety. The Trial's secondary endpoint was efficacy, although the Trial was ***not*** powered to show statistical significance as to efficacy.

123. Phase 2a of the Trial was designed to span one year before results would be publicly reported. On the first week of the Trial patients in the treatment arm were to receive a subretinal injection of AVA-101, and thereafter, beginning on the eighth week of the Trial, study visits were to occur every 4 weeks for 52 weeks. During these follow-up visits patients in both the treatment arm and the control arm were eligible to receive injections of a standard therapy, *i.e.* "rescue injections," if their Wet AMD symptoms worsened.

124. Rescue injections were provided to patients when pre-specified criteria for any one of the following were reached: vision decreased, retinal thickening was observed, or retinal fluid leakage was detected. These three measures, along with the number of rescue injections required,

were not only the efficacy endpoints for the Trial, they were also measured by the same methods that were used to observe ocular safety, the safety endpoint for the Trial. Therefore, the safety data would have indicated whether AVA-101 was effective in patients.

125. As patients progressed through Phase 2a of the Trial, data from each monthly visit was gathered and compiled into a database as part of the safety surveillance program required by federal regulation. This data was periodically reviewed by the Trial's safety data monitoring committee; indeed in June 2014, an interim analysis was conducted.

126. Phase 1 involved 8 patients and was fully enrolled by April 2012. Phase 2a involved 32 patients and began enrollment in April 2012. During the course of the first year of the Phase 1 Trial, Avalanche and LEI periodically reviewed and reported safety data for the 8 patients enrolled. For example, in May 2012 Avalanche and LEI reported the 8-week safety data for Phase 1 patients; in May 2013 Avalanche and LEI reported a 10-month progress report with safety data for Phase 1 patients; and in June 2013 Avalanche and LEI reported the safety results from the subretinal injection in 17 patients enrolled in the AVA-101 Trial, ***which included 9 patients enrolled in Phase 2a***.

127. By February 8, 2014, Phase 2a of the AVA-101 Trial was fully enrolled. Two months later, after reviewing the exceptional results from Phase 1 of the AVA-101 Trial, Avalanche embarked on its public relations campaign to launch a public offering based upon the enthusiasm generated from these results and profit handsomely.

128. To carry out this blitz, beginning in April 2014, a year after the results became available, Avalanche and LEI began to publicize the remarkable 52-week Phase 1 results. In presentations, news articles, and trial abstracts, LEI and Avalanche announced that in Phase 1 AVA-101 had the desired effect in the treatment arm as on average ***retinal thickness decreased by 200 um***,[14] ***visual acuity increased by 7.5 letters***, and ***5 of 6 patients in the treatment arm did not receive any rescue injections***, as ***out of a possible 72 rescue injections, only 2 rescue injections***

[14] "Um" is the International System of Units' symbol for a micrometer or microns. *See Micrometre*, Wikipedia, https://en.wikipedia.org/wiki/Micrometre (last visited Dec. 1, 2016).

were given. These results provided hope that one subretinal injection of AVA-101 might cure Wet AMD because nearly every patient was able to maintain stable vision without the need for a rescue injection for an entire year.

129. In the midst of this media blitz, Avalanche received interim safety surveillance data which would have contained sufficient data to indicate that AVA-101 was not having the desired effect in patients in Phase 2a of the Trial, including at the very least 8-week data for all patients. Specifically, within the first 8 weeks of treating patients in Phase 2a, data showed that retinas were thickening for patients in the treatment arm and thinning for patients in the control arm by a difference of 81 um—the opposite of what you would see with an effective drug—and this delta remained constant throughout the Trial. Also, full 1-year data would have most likely been available for 21 of 32 patients by July 2014, 6-month or greater data would have been available for the remaining 8 patients enrolled in the latter half of 2013, and 4-month or greater data for the two patients who enrolled in 2014. This amount of data would have been sufficient to indicate that the retinas of patients in the treatment group were thickening and patients in the treatment arm were receiving rescue injections at a materially greater rate than patients in Phase 1. Thus revealing that AVA-101 was not a material improvement over the standard of care, would not be a functional cure via one subretinal injection, and would not justify a more invasive procedure.

130. The interim safety data, however, was not the only data that the Exchange Act Defendants would have reviewed during the course of Phase 2a of the Trial. Based upon the periodic safety data reported during the course of Phase 1 (*i.e.*, the 8-week data reported in May 2012, the progress report in May 2013, and the 17 patient data reported in June 2013) the Trial protocol permitted interim review of at least the safety data throughout the course of the Trial, including by Avalanche. Indeed, some time before June 2013 Avalanche, Chalberg, and Blumenkranz viewed the safety data for 9 patients in Phase 2a and published an analysis in a trial abstract.

131. To carry out the second part of the plan, Avalanche launched its initial public offering ("**IPO**") on July 30, 2014, issuing 6.9 million shares and raising $106.8 million, after deducting underwriting discounts and commissions and estimated offering expenses.

132. For the remainder of 2014, the Exchange Act Defendants continued to tout the safety and efficacy of AVA-101 as a treatment for Wet AMD in presentations and public filings. As a result of the enthusiasm generated by Avalanche's publicity, the price of Avalanche's common stock soared to a market high in December 2015. The Company decided to reap the rewards of its efforts and launched a secondary offering on January 7, 2015, selling 2,759,375 shares for a total of $130.5 million, after deducting underwriting discounts and commissions and estimated offering expenses. Armed with the negative Phase 2a data, Avalanche insiders decided to take advantage of the one exception to the IPO lock-up period and sold a total of 290,000 shares of their personal holdings of common stock for total proceeds of $16,083,400, which constituted more than 10% of all the shares sold in the offering.

133. The Avalanche insiders abandoned ship just in time. On June 15, 2015, the Exchange Act Defendants announced the one-year results from Phase 2a of the AVA-101 Trial and ultimately had to admit that the Trial showed that AVA-101 was not effective in treating Wet AMD. The results revealed that in many cases, the patients in the treatment arm fared worse than those in the control arm. Indeed, the retinas of the treatment arm thickened by 25 um whereas the retinas of the control arm thinned by 56 um; and the treatment arm received an average of 3.1 rescue injections, with 47% of patients receiving between 3 and 7 rescue injections, whereas the control arm received an average of 3.6 rescue injections, with patients receiving between 2 and 5 rescue injections. These results were an utter failure compared to Phase 1 of the Trial where 5 of 6 patients received 0 rescue injections and retinas decreased in the treatment group by 200 um, and did not justify the heightened risks of subretinal injections.

134. The results from Phase 2a were not well received by the market. Two analysts cut their price projections for the Company by more than half, and several other investor publications criticized the results, with one going so far as to state that "I'm struggling to adequately describe the

awfulness of Avalanche Biotechnologies' [] performance Monday night[.]" On these results, Avalanche common stock plummeted more than 56%, closing on June 16, 2015 at $17.05 per share. A month after this announcement Chalberg resigned as CEO and president.

135. Several months later, Avalanche was forced to face the facts and decided to discontinue development of AVA-101 based upon the lack of efficacy shown in Phase 2a of the Trial. Indeed, the results were so poor that further development was not warranted ***even though Phase 2a was not powered to show statistical significance of efficacy***.

136. The true facts, which were known and/or recklessly disregarded by the Exchange Act Defendants but concealed from the investing public during the Class Period, were that beginning in at least June 2014, the Exchange Act Defendants knew and/or recklessly disregarded and failed to disclose that:

a) patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening of the retina, evidencing that AVA-101 was not effective in treating Wet AMD;

b) patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD; and

c) as a result, Avalanche's business and financial prospects concerning AVA-101 were not what the speakers had led the market to believe they were.

137. As a result of the Exchange Act Defendants' wrongful acts and omissions, and the precipitous decline in the market value of the Company's common stock when the true facts came to light, Bachhawat and other relevant Class Members have suffered significant losses and damages.

138. These claims brought under the Exchange Act are asserted against Avalanche and certain of its officers and directors, who, during the Class Period, made materially false or misleading statements or omissions in press releases, presentations, analyst reports, and filings with the SEC, that operated as a fraud or deceit upon Bachhawat and other relevant members of the Class.

VI. THE EXCHANGE ACT PARTIES

A. The Exchange Act Plaintiff

139. Lead Plaintiff Arpan Bachhawat, as set forth in his shareholder certification (ECF No. 26-3), purchased Avalanche common stock at artificially inflated prices during the Class Period and was damaged thereby. Lead Plaintiff Bachhawat is referred to herein as the "**Exchange Act Plaintiff**."

B. The Exchange Act Defendants

1. The Company

140. Defendant Avalanche was a Delaware corporation with its principal executive offices located at 1035 O'Brien Drive, Suite A, Menlo Park, California 94025. Avalanche was a biopharmaceutical company that uses its proprietary Ocular BioFactory™ platform to discover and develop novel treatments for ophthalmic diseases. During the Class Period, the Company's stock was traded on the NASDAQ Global Select Market ("**NASDAQ**") under the symbol "AAVL."

2. The Individual Exchange Act Defendants

141. Defendant Chalberg co-founded Avalanche, and, until his resignation on July 23, 2015, was the Chief Executive Officer ("**CEO**"), president, and a member of the Board of Directors of Avalanche. Because of his positions with the Company, Chalberg had access to all the Company's study protocols, patient data, updates, outcomes, and results. Chalberg directly participated in and controlled the management of the Company, including, without limitation, the publication of statements by and on behalf of Avalanche concerning AVA-101 in the Company's press releases, SEC filings, and other public statements. Chalberg was motivated by the financial implications of the IPO and the 2015 Offering (defined below) and personally sold at least 135,000 shares of Avalanche common stock during the Class Period, receiving over $6,415,145 in proceeds.

142. Defendant Bain was the Chief Financial Officer ("**CFO**") of Avalanche until her resignation on October 19, 2015. Because of her position with the Company, Bain had access to all the Company's study protocols, patient data, updates, outcomes, and results. Bain directly

participated in and controlled the management of the Company, including, without limitation, the publication of statements by and on behalf of Avalanche concerning AVA-101 in the Company's press releases, SEC filings, and other public statements. Bain resigned from the Company on October 19, 2015. Bain was motivated by the financial implications of the IPO and the 2015 Offering and personally sold at least 7,000 shares of Avalanche common stock during the Class Period, receiving over $253,659 in proceeds.

143. Defendant Blumenkranz co-founded Avalanche and, at all relevant times, was the Chairman of the Board of Directors of Avalanche. Because of his position with the Company, Blumenkranz had access to all the Company's study protocols, patient data, updates, outcomes, and results. Blumenkranz directly participated in and controlled the management of the Company, including, without limitation, the publication of statements by and on behalf of Avalanche concerning AVA-101 in the Company's press releases, SEC filings, and other public statements. Blumenkranz was motivated by the financial implications of the IPO and the 2015 Offering and personally sold at least 231,000 shares of Avalanche common stock during the Class Period, receiving over $10,417,890 in proceeds.

144. Defendant Schwartz co-founded Avalanche and, at all relevant times, was a member of Avalanche's Board of Directors. Because of his position with the Company, Schwartz had access to all the Company's study protocols, updates, outcomes, and results. Schwartz directly participated in and controlled the management of the Company, including, without limitation, the publication of statements by and on behalf of Avalanche concerning AVA-101 in the Company's press releases, SEC filings, and other public statements. Schwartz was motivated by the financial implications of the IPO and the 2015 Offering and personally sold at least 193,375 shares of Avalanche common stock during the Class Period, receiving over $9,000,000 in proceeds.

145. Defendants Chalberg, Bain, Blumenkranz, and Schwartz are collectively referred to hereinafter as the "**Individual Exchange Act Defendants**" and together with Avalanche they are referred to herein as the "**Exchange Act Defendants**."

146. The Individual Exchange Act Defendants, because of their positions with the Company, possessed the authority to control, correct, and/or update the contents of Avalanche's public disclosures to the market. Each of the Individual Exchange Act Defendants had the duty to exercise due care and diligence and the duty of full and candid disclosure of all material facts relating to the Company's financial results and operations. The Individual Exchange Act Defendants further had the duty to correct and/or update any previously issued statements that were untrue or became materially misleading or untrue, so that the market price of the Company's publicly traded common stock would be based upon truthful, complete, and accurate information. To discharge their duties, the Individual Exchange Act Defendants were required to exercise reasonable and prudent supervision over the dissemination of information concerning the Company's financial results and operations. By virtue of such duties, these officers and directors were required, *inter alia*, to:

a) conduct and supervise the business of Avalanche in accordance with federal laws;

b) supervise the preparation of Avalanche's SEC filings and approve any reports concerning Avalanche's financial reporting and results; and

c) ensure that Avalanche established and followed adequate internal controls.

147. As officers, directors, and/or controlling persons of a publicly-held company which is registered with the SEC under the federal securities laws and the securities of which were traded on the NASDAQ and governed by the provisions of the federal securities laws, the Individual Exchange Act Defendants each had a duty to (1) promptly disseminate complete, accurate and truthful information with respect to the Company's financial statements and operations; (2) correct any previously issued statements that were materially misleading or untrue so that the market could accurately price the Company's publicly traded securities based upon truthful, accurate, and complete information; and (3) update any previously-issued statements that became materially misleading or untrue so that the market could accurately price the Company's publicly traded securities based upon truthful, accurate, and complete information.

148. The Individual Exchange Act Defendants are each primarily liable for the misrepresentations and misleading statements alleged herein and are also liable as controlling persons of Avalanche. The Individual Exchange Act Defendants omitted material information regarding Avalanche's AVA-101 Trial, which caused Plaintiffs and other members of the Class to purchase Avalanche common stock at artificially inflated prices during the Class Period and suffer damages as a result.

VII. BACKGROUND OF THE EXCHANGE ACT CLAIMS

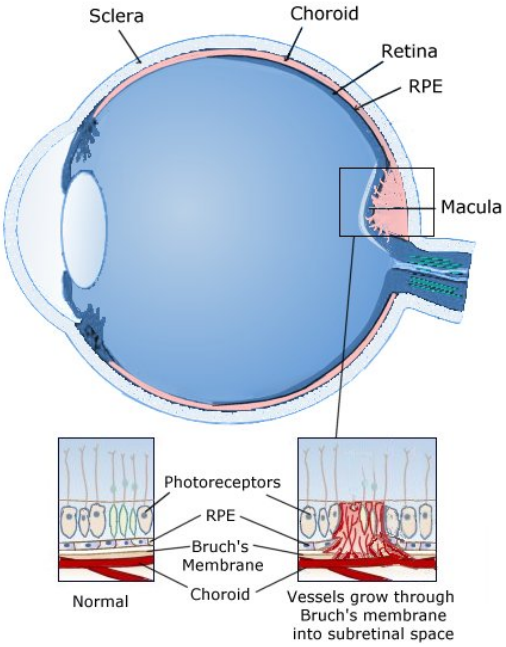
A. Background of the Company, Wet AMD, and AVA-101

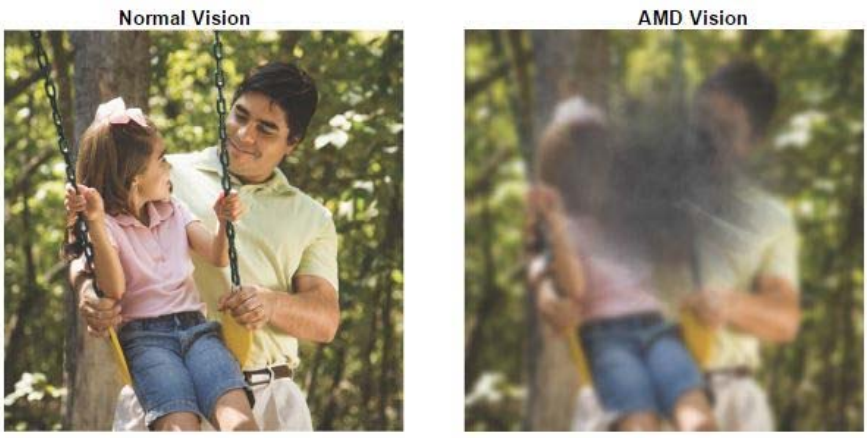
149. Avalanche is a biopharmaceutical company focused on the development and commercialization of a gene therapy platform, dubbed its Ocular BioFactory™ platform, which is designed to treat ophthalmic diseases. *See The Ocular BioFactory™*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/the-ocular-biofactory.php (last visited Jan. 29, 2016). Avalanche's Ocular BioFactory™ platform consists of treatments that use the adeno-associated virus ("**AAV**") as a vector to deliver and express a functional gene to the cells of the eye to promote continuous production of a certain protein. *See id.*

150. Avalanche's lead AAV vector was AVA-101, a/k/a rAAV.sFlt-1, which was being developed to treat Wet AMD. *See* Ex. B, the 2014 Registration Statement. AMD is a progressive disease affecting the cells in the macula, which is an oval-shaped pigmented area that forms the center of the retina and is the region of the eye responsible for central vision. *See About Age-Related Macular Degeneration*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/about-amd.php (last visited Jan. 18, 2016).

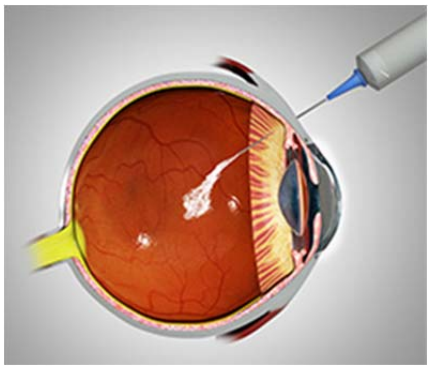
151. Wet AMD is an advanced form of AMD whereby patients suffer from debilitating vision loss and loss of the ability to perform daily activities. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 14 (2015). ***Wet AMD occurs when the membrane underlying the retina thickens, then breaks***. *See Wet AMD*, The Macular Degeneration Partnership, https://www.amd.org/what-is-macular-degeneration/wet-amd/ (last visited Jan. 29, 2016). The oxygen supply to the macula is disrupted and the body responds by

growing new, abnormal blood vessels, which is known as choroidal neovascularization ("**CNV**"). *See id.*; *see also Wet Macular Degeneration (AMD)*, American Macular Degeneration Foundation, https://www.macular.org/wet-amd (last visited Jan. 29, 2016). These new blood vessels are very fragile and often leak and bleed, which results in excess fluid in the retina causing swelling—*i.e.*, thickness of—the retina. *See Wet AMD*, The Macular Degeneration Partnership, https://www.amd.org/what-is-macular-degeneration/wet-amd/ (last visited Jan. 29, 2016). The leakage from these blood vessels also damages photo receptors, which results in rapid vision loss. *See id.* A diagram of this process and a demonstration of the type of vision loss experienced are set forth below:



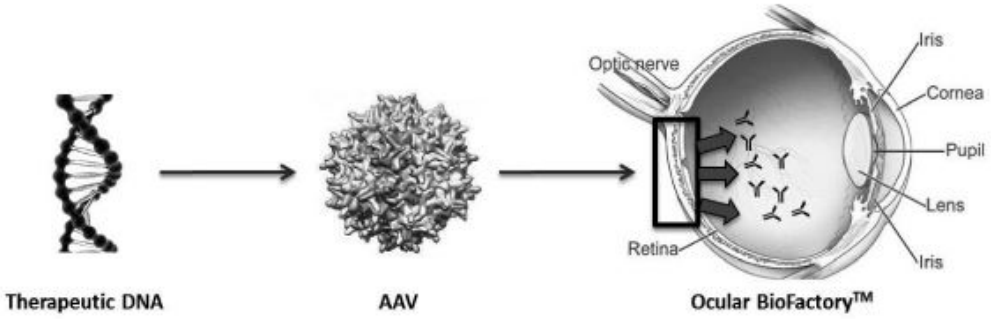


152. Vascular endothelial growth factor ("**VEGF**") is a protein known to play a central role in the growth of the new blood vessels in the retina. *See Current Treatments*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/current-treatments.php (last visited Jan. 18, 2016). A number of FDA-approved therapies have been developed to block the effects of VEGF by binding to and sequestering the protein, causing the new blood vessels to shrink. *See id.* The most common FDA-approved anti-VEGF treatments are (1) Lucentis® (ranibizumab), marketed by Genentech, Inc. and Novartis AG, which is an antibody fragment that binds to and inhibits VEGF proteins in the eye; (2) EYLEA®, marketed by Regeneron Pharmaceuticals, Inc., which is a recombinant fusion protein containing portions of the human VEGF receptor that binds to soluble VEGF; and (3) Avastin®, marketed by Genentech, Inc., which is an antibody that binds to VEGF. *See id.* These existing treatments are administered through ***intravitreal injections***, which are injections into the center of the eye after administration of ***topical anesthesia***, depicted as follows:

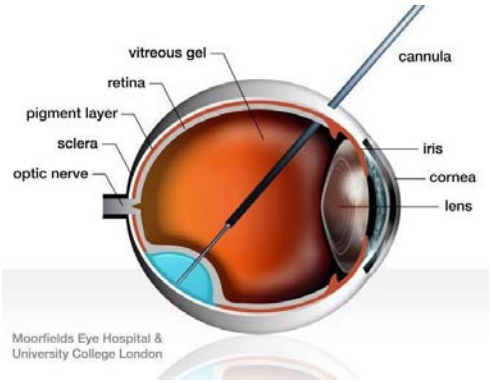


153. Because these biologic agents decay over time, causing "peaks" and "troughs" of VEGF inhibition, ***standard treatments require injections every 4 to 8 weeks to maintain stable vision***. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 14 (2015). While these therapies have proven to be effective in treating the symptoms of Wet AMD, the frequency and discomfort of administration is burdensome for patients, leading many to terminate treatment or not comply with the prescribed regimen, resulting in vision loss. *See id.*

154. In contrast to the current standards of care, which are laboratory-manufactured antibodies, AVA-101 purported to be a novel gene therapy. This gene therapy utilized a viral vector to carry the desired genetic information—nucleic acids that encode a protein of interest—to target cells and cause them to utilize the cell's machinery to express the protein of interest. *See* Aaron Shapiro, *Gene Therapy for Retinal Diseases*, Retina Today, April 2015, at 24. The goal of gene therapy is to provide a sustained therapeutic benefit via continual expression of the protein of interest. *See id.* AVA-101 is comprised of the AAV2 vector, which contains a gene encoding sFLT-1, a naturally occurring anti-VEGF protein. *See* 2014 Registration Statement at 81. Avalanche hypothesized that when administered in the eye and expressed by the host retinal cells, the sFLT-1 protein would inhibit the formation of new blood vessels and blocks VEGF activity. *See id.* A diagram of how AVA-101 was intended to operate in the eye is included below:

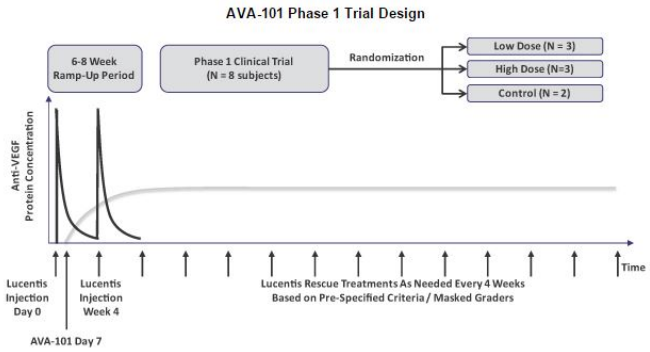


155. ***Unlike the current FDA-approved therapies, AVA-101 was designed to be administered through a <u>single subretinal injection</u>***. *See* Ex. B, 2014 Registration Statement at 81. Subretinal injections are injections through the middle of the eye, directly into the retina in the back of the eye, depicted as follows:



156. The purpose of this type of highly invasive injection is to place the vector in direct contact with the retinal cells to enhance protein expression. *See id.* ***Subretinal injections are more difficult to administer and more invasive than intravitreal injections, requiring an operating room and anesthesia***. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 23 (2015). ***They are also subject to more adverse safety events*** such as "the development of a retinal hole at the site of entry through the retina, reflux of the therapeutic agent back into the vitreous cavity, potentially decreasing efficacy or scar formation from proliferation of cells on the retinal surface, and prolonged retinal detachment." Biren Amin, Jefferies, *Initiate at Buy: AAVL Gene Therapy Has Disruptive Potential in Wet AMD*, 16-17 (Aug. 25, 2014). An analyst at Cowen & Co. stated that "AVA-101 is delivered through a more cumbersome subretinal procedure, and therefore our consultant thinks it needs to either provide meaningfully better efficacy, or result in a significantly diminished subsequent injection burden, in order to be competitive." Phil Nadeau, Cowen & Company, *Ph. IIa Demonstrates Safety and Activity, Though Doesn't Define 101's Role*, 1 (June 16, 2015).

157. If effective, AVA-101 could result in sustained production of a natural inhibitor of VEGF, and therefore stabilize cellular levels of VEGF. ***Thus, a <u>one-time</u> subretinal injection of AVA-101 was designed to introduce a lasting source of VEGF inhibition in the eye and enable constant prevention of new blood vessel formation, eliminating the need for intravitreal injections every 4 to 8 weeks***. *See* Salveen Richter, SunTrust Robinson Humphrey, *An Eye To a Cure, Initiating with a Buy and $60 PT*, 14 (2015). A graphic of the difference in intended anti-VEGF effect between standard therapies and AVA-101 is as follows:



B. The Phase 1/2a AVA-101 Trial Design

158. Research and development of the science behind AVA-101 began more than 20 years ago, spearheaded by Professor Elizabeth Rakoczy ("**Rakoczy**") at LEI, an ophthalmic research organization based in Perth, Australia. *See* Lions Eye Institute, Annual Report, 34 (2013). Over the years, close to 100 scientists, ophthalmologists, veterinarians, virologists, and PhD students participated in the project. *See id.* From 2002 to 2007 a grant from the National Health and Medical Research Council enabled the research team to take the basic research project to the clinical trial phase. *See id.*

159. LEI began collaborating with Avalanche on its AVA-101 research in approximately 2008. *See* Lions Eye Institute, Annual Report, 10 (2014). "Following an approval from the . . . TGA – the know-how and associated data" for AVA-101 "were acquired by Avalanche . . ." Lions Eye Institute, Annual Report, 35 (2013). Thus, in March 2010, Avalanche entered into a research collaboration agreement with LEI whereby Avalanche licensed certain intellectual property rights in LEI's ophthalmology platform, including the rights to develop AVA-101. *See* Avalanche Biotechnologies, Inc., Registration Statement (Form S-1), F-22 (2015) ("**2015 Registration Statement**"). Under the terms of the agreement, LEI agreed to conduct certain clinical research studies and Avalanche committed to funding the research and issued LEI warrants to purchase 400,000 shares of Avalanche common stock. *See id.* In October 2010, Rakoczy and Professor Ian Constable ("**Constable**")—***the individuals responsible for developing AVA-101 at LEI—were then appointed as the Chairs of Avalanche's Scientific Advisory Board and Clinical Advisory Board, respectively***. *See Scientific Advisory Board*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/scientific-advisory-board.php (last visited Jan. 29, 2016); *Clinical Advisory Board*, Avalanche Biotechnologies, Inc., http://www.avalanchebiotech.com/clinical-advisory-board.php (last visited Jan. 29, 2016).

160. Shortly thereafter, Chalberg and Schwartz collaborated with Rakoczy and Constable to create the study design and seek regulatory approval of a multi-phase trial to test AVA-101 in human patients. *See* Ex. C, Lancet at 2402.

161. The AVA-101 Trial was registered with the Therapeutics Goods Administration ("**TGA**") which is Australia's analog to the U.S. Food and Drug Administration ("**FDA**"). To conduct a gene therapy trial in Australia, a sponsor must first submit the proposed trial protocol to the applicable Human and Research Ethics Committee ("**HREC**")[15] and the National Health and Medical Research Counsel ("**NHMRC**"). *See* Therapeutic Goods Administration, *Access to Unapproved Therapeutic Goods*, 18 (2004). Once the HREC and NHMRC approve the protocol, the sponsor submits an application under the Clinical Trial Exemption Scheme to the TGA for approval. *Id.*

162. After the TGA approved the application for the AVA-101 Trial, on December 14, 2011, Avalanche filed with www.clinicaltrials.gov[16] an overview of the trial protocol ("**Trial Overview**") for the AVA-101 Trial which was entitled "A Phase I/II Controlled Dose-escalating Trial to Establish the Baseline Safety and Efficacy of a Single Subretinal Injection of rAAV.sFlt-1 Into Eyes of Patients With Exudative Age-related Macular Degeneration (AMD)" (the AVA-101 Trial), identifier number NCT01494805. *See* Ex. D, Trial Overview.

163. The AVA-101 Trial was arranged to take place in Australia at Sir Charles Gairdner Hospital with LEI acting as the trial investigator. Constable was the Principal Clinical Investigator and performed the subretinal injections on each patient. *See* Elizabeth Rakoczy, Lion's Eye Institute, *Application for Funding: Project Grants 2010 round – for funding 2011*, 7-8 (2010). He was also responsible for all aspects of the participants' welfare and clinical data interpretation, and supervising the collectors of clinical data and imaging. *See id.* Rakoczy was responsible for liaising with clinical, statistical, and research staff, data management and interpretation, and liaising with patients if necessary. *See id.* Dr. Chooi-May Lai ("**Lai**"), another doctor on the team at LEI, managed the data generated and interpreted the results from the trial. *See id.*

[15] The institution where the trial will be conducted has an HREC that assesses the scientific validity of the trial design, the safety and efficacy of the medicine and the ethical acceptability of the trial process. Here, the HREC was based at Sir Charles Gairdner Hospital in Nedlands, Australia, which is the only testing site for the trial and regularly serves as LEI's patient treatment facility. *See* Ex. C, Lancet at 2397.

[16] Clinicaltrials.gov is a website established by the National Institutes of Health.

164. Avalanche and LEI were both sponsors of and collaborators on the study. *See* Ex. E, LEI 2012 Annual Report at 20; Ex. F, Trial Review; No. 74 at 6, ECF No. 105 at 7. Despite LEI acting as the principal investigator, both entities considered the AVA-101 Trial to be Avalanche's study. Lions Eye Institute, Annual Report, 9 (2014). Avalanche repeatedly stated that it was "***evaluating AVA-101 in a Phase 1/2a*** trial at LEI in Australia[,]" 2015 Registration Statement at 84, and LEI stated in its 2014 Annual Report that "***Avalanche is conducting clinical trials of a treatment for age-related macular degeneration*** – leveraging ground breaking research conducted over many years by LEI[.]" Lions Eye Institute, Annual Report, 9 (2014).

165. The trial was a single-center, open-label[17] study that was designed to consist of patients aged 65 or above who have Wet AMD. *See* Ex. D, Trial Overview at 1; Thomas W. Chalberg, CEO, Avalanche Biotechnologies, Inc., AVA-101 Phase 2a Study Results Call, 3 (June 15, 2015) (transcript on file with Bloomberg, Inc.). Patients were sequentially randomized to either receive a dose of AVA-101 or to be assigned to the control group. *See id.* at 1. Patients in both groups were eligible to receive rescue therapy with ranibizumab as needed. *See* Ex. D, Trial Overview at 3.

166. The AVA-101 Trial was one study broken into two phases (Phase 1 and Phase 2a). *See id.* at 2. ***The AVA-101 Trial was conducted under a single trial protocol which was meant to apply to all 40 patients and provided, inter alia, for the same endpoints for both phases***. *See* Webcast: *Avalanche Biotechnologies Analyst and Investor Day* (Mar. 25, 2015), http://investors.adverumbio.com/phoenix.zhtml?c=253634&p=irol-EventDetails&EventId=5183324 ("[T]he reinjection criteria for the Phase 2a are identical to the Phase 1. And those are based on visual acuity, OCT, and fluorescein angiography. And so any increases in that activity would warrant a rescue treatment.").[18]

[17] An open-label trial is the type of trial where both the investigators and the subjects know which treatment is being administered.

[18] *Accord*, Ex. D, Trial Overview (trial is intended to treat 40 patients); Ex. F, Trial Review; Lions Eye Institute, Spring Newsletter, 3 (2014); Ex. J, *Ocular Gene Therapy Showed*

167. The primary endpoint of the AVA-101 Trial—the "safety endpoint"—was to measure "ophthalmic safety" by ensuring there were no signs of unresolved ophthalmic complications, toxicity or systemic complications as measured by laboratory tests from 1 month post injection. *See id.* at 15. "Ophthalmic safety"[19] was to be determined by reviewing abnormal laboratory data and conducting an ocular examination of (a) ocular inflammation; (b) intraocular pressure; (c) ***visual acuity ("BCVA")***; and (d) ***retinal bleeding***.[20] *See id.* at 15. Ophthalmic safety was assessed by using biomicroscopy, indirect ophthalmoscopy, ***Spectral Domain Optical Coherence Tomography ("SD OCT")***, Color Fundus (retinal) Photography (CFP),[21] and ***Fluorescein Angiography ("FA")***. *See* Ex. E, Elizabeth P. Rakoczy, et al., *The First Report on a rAAV.sFlt-1 Phase I/II Trial for Wet Age-Related Macular Degeneration (AMD)* (2012) (Discussing safety, stating "[a]t day 60 none of the patients required rescue treatment. ***There was no evidence of visual acuity loss,*** IOP elevation, retinal detachment, or any intraocular or systemic immune response in any of the patients."); *see also* Ex. H, April 2014 Abstract ("***Ophthalmic safety was assessed by*** biomicroscopy, IOP, indirect ophthalmoscopy, ***SD OCT***, CFP and ***FA***."); Ex. C,

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Fewer Injections Needed, Increased Visual Gain, Retina Today (2014), http://retinatoday.com/2014/04/ocular-gene-therapy-showed-fewer-injections-needed-increased-visual-gain ("Dr. Charlberg said that an ongoing phase 2A study currently has 40 patients enrolled."); Ex. E, LEI 2012 Annual Report at 20 (by end of 2012, 20 patients had been enrolled in the Trial); *See* Ex. K, Ian Constable, et al., *Anti-VEGF Gene Therapy for Wet AMD: Safety and Tolerability of Subretinal Delivery in a Phase I/II Clinical Trial*, 54 IOVS 4504 (2013) (analysis of the subretinal injection in 17 patients); Nancy Groves, *Long-term gene therapy for wet AMD promising: One year follow-up on rAAV.sFt-1 finds no evidence of inflammation, IOP elevation, events, clinical changes*, Ophthalmology Times, July 15, 2014 (Analysis for first "8 of 40 subjects enrolled").

[19] *See* Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (June 15, 2015) ("Phase 2a clinical study for AVA-101 met its 12-month primary endpoint, based on ophthalmic and systemic safety[.]"); Avalanche Biotechnologies Inc., Quarterly Financial Report (Form 10-Q), 16 (Nov. 9, 2015) ("The primary endpoint of the Phase 2a study was based on ophthalmic and systematic safety[.]").

[20] Retinal bleeding, or vitreous hemorrhaging, is detected through SD OCT. *See Vitreous Hemorrhage*, Retina Eye Specialists, http://www.retinaeye.com/vitreoushemorrhage.html (last visited Nov. 10, 2016).

[21] Color fundus (retinal) photography simply takes a color picture of the back of the eye, including the macula.

Lancet at 2402 ("***Ocular safety was monitored at each monthly visit with BCVA***, intraocular pressure, slit lamp biomicroscopy, indirect ophthalmoscopy, and ***SD-OCT***[.]").

168. The secondary endpoint of the AVA-101 Trial—the "efficacy endpoint"—was to determine the maintenance or improvement of vision ***without the need for ranibizumab rescue injections***. This was to be measured by (a) ***best-corrected visual acuity (BCVA)***; (b) CNV lesion (a/k/a fluid leakage), ***detected using FA***;[22] and (c) foveal thickness (a/k/a retinal thickness), ***detected using SD OCT***. *See* Ex. C, Trial Overview at 15. A chart displaying the two sets of endpoints is set forth below:

Primary Endpoint—Safety Measures	**Secondary Endpoint—Efficacy Measures**
visual acuity (BCVA)	visual acuity (BCVA)
Spectral Domain Optical Coherence Tomography (SD OCT)	retinal thickness detected by SD OCT
Fluorescein Angiography (FA)	CNV lesions a/k/a fluid leakage detected through FA
biomicroscopy	rescue injections
indirect ophthalmoscopy	
Color Fundus (retinal) Photography (CFP)	
ocular inflammation	
intraocular pressure (IOP)	
retinal bleeding	

169. ***Contrary to what Defendants previously led the Court to believe without any basis*** (ECF No. 105 at 6), ***the AVA-101 Trial was not powered to show statistically significant results for efficacy***. Chalberg himself explained this stating: "Our Phase 2a trial is a safety study . . . This

[22] A CNV lesion is the area of the macula where the new blood vessels have begun to form. The presence and size of CNV lesions are determined by looking at the leakage patterns on a fluorescein angiography image (defined below). *See* Amitha Domalpally, et al., *Fluorescein Angiography in Neovascular AMD: An in-depth look at FA's role in detailing lesion composition and characteristics*, Review of Ophthalmology (2008). The statements made by LEI and Avalanche often discuss "FA" or "leakage" and this is all related to determining the presence of CNV lesions.

study is not powered for statistical significance of secondary endpoints." Interview with Dr. Thomas Chalberg, CEO, and Dr. Mark Blumenkranz, Chairman of the Board, Avalanche Biopharmaceuticals, Inc., *via* e-mail (May 22, 2015), *available at* http://seekingalpha.com/article/3205796-avalanche-management-addresses-wall-streets-concerns-ahead-of-binary-catalyst. Rakoczy also stated the following: "This study was designed as a phase 1 study to assess the safety of the subretinal procedure and rAAV.sFLT-1. Hence, it was not powered to draw definitive conclusions about differences in efficacy between groups." Ex. C, Lancet 2403.

170. During the Trial, all subjects were to receive two initial doses of ranibizumab at Day 0 and Week 4 and the subjects in the active arms received AVA-101 on Day 7. *See* 2014 Registration Statement at 83. Beginning with the Week 8 visit, ranibizumab was to be given as rescue therapy on an as-needed basis. *See id.* ***This date was chosen because after 8 weeks, the period of time was adequate for protein expression to develop from the AVA-101 injection***. *See* Ex. C, Lancet at 2396.

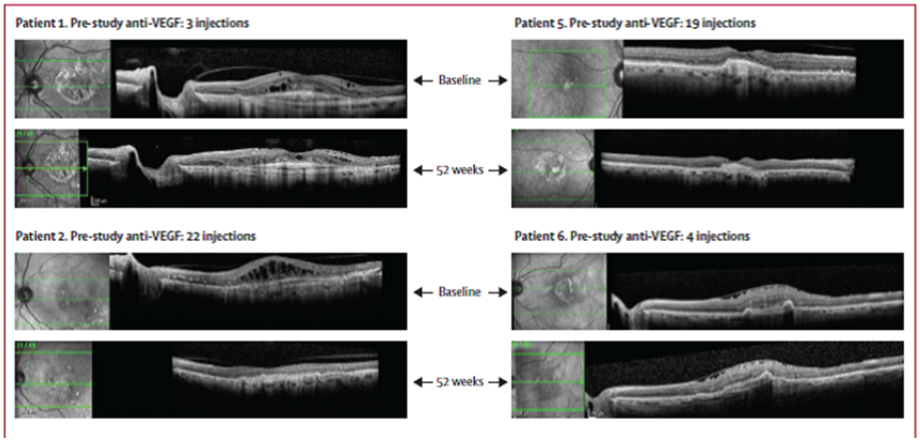
171. According to Rakoczy:

> Rescue treatment with ranibizumab was given when active choroidal neovascularization progression was detected, as measured by: (1) loss of ten or more letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale from previous visit, or loss of five or more letters from previous visit on ETDRS scale in conjunction with patient perception of functional loss where such loss is attributable to choroidal neovascularisation; (2) any choroidal neovascularization related increased subsensory, intraretinal, or sub-RPE fluid on OCT; or (3) signs of increased choroidal neovascularisation leakage on FA.

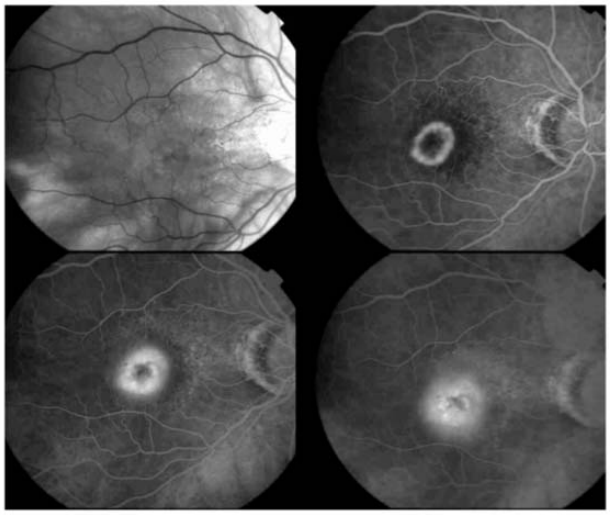
Ex. C, Lancet at 2397. In general terms, this means that rescue injections were based upon pre-specified levels of (1) worsening visual acuity, (2) increases in retinal thickness, and (3) increases in CNV fluid leakage. *See id.* at 2398, 2399, & 2400 (Describing "[b]aseline best corrected visual acuity" by "ETDRS Letters"; discussing retinal thickness results; and describing FA assessments as showing no "recurrence of leakage"). These pre-specified criteria for rescue therapy were chosen to "***assess signals of efficacy***, ***protect patient safety***, and to assess the long term treatment effect" of AVA-101. Ex. C, Lancet at 2397.

172. Visual acuity is the clearness or sharpness of vision measured at the distance of 20 feet. *See Visual Acuity: What is 20/20 Vision?*, American Optometric Association, http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/visual-acuity?sso=y (last visited Jan. 29, 2016). As explained by Rakoczy, the Early Treatment Diabetic Retinopathy Study ("**ETDRS**") scale, which is a standard eye chart characterized by rows of letters decreasing in size, was used to measure visual acuity in the AVA-101 Trial. *See* Ex. C, Lancet at 2397. An example of the ETDRS scale is included below:

173. Retinal thickness is increased when there is a buildup of fluid in the retina. The fovea is the largest concentration of cone cells in the eye located in a small pit in the center of the retina. *See* Abstract, Adaptation of the Central Retina for High Acuity Vision: Cones, the Fovea and the Avascular Zone, *available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658155/. In the AVA-101 Trial retinal thickness was measured by Spectral Domain Optical Coherence Tomography, SD-OCT which is a non-contact medical imaging technology similar to an ultrasound or MRI that takes 3-D cross-sectional images of the retina. Zahid Yaqoob, et al., *Spectral domain optical coherence tomography: a better OCT imaging strategy*, 39 BioTechniques S6 (2005); Press Release, Avalanche Biotechnologies, Inc., *Avalanche Biotechnologies, Inc. Announces Positive Top-Line Phase 2a Results for AVA-101 in Wet Age-Related Macular Degeneration* (June 15, 2015) ("mean change from baseline in retinal thickness as measured by SD-OCT"). SD-OCT images of the retinas of several patients treated in the AVA-101 Trial are included below:



174. Fluid leakage into the retina was detected through a fluorescein angiography ("FA") test. *See* Ex. C, Lancet at 2400; *Fluorescein Fundamentals*, Ophthalmic Photographers' Society, http://www.opsweb.org/?page=FA (last visited Jan. 29, 2016). FA is performed by injecting a fluorescent dye into a peripheral vein. *See id.* Then, as the dye courses through and highlights the blood vessels in the eye, a specialized fundus camera or scanning laser ophthalmoscope is used to capture rapid-sequence photographs of the retina to determine the presence of blood vessel leakage. *See id.* Below are FA images of patients with Wet AMD:



175. These three measures—(1) worsening visual acuity, (2) increases in retinal thickness, and (3) increases in CNV fluid leakage—are the mostly commonly accepted measures used to determine whether a drug is inhibiting VEGF and causing an anti-VEGF response in the

eye; therefore, they are not only the criteria for giving rescue injections in standard practice—not so coincidentally—they are also the three measures used to determine the secondary endpoint of efficacy. *See* Aetna No. 0701, *Vascular Enothelial Growth Factor Inhibitors for Ocular Indications*, *available at* http://www.aetna.com/cpb/medical/data/700_799/0701.html. Because rescue injections were given to patients in the AVA-101 Trial based upon pre-specified criteria for these three measures, a cursory review of the efficacy data collected would indicate how many rescue injections were given to each patient.

176. The Company attempted to separate the results from the AVA-101 Trial into "safety" and "efficacy" endpoints; however, a closer look makes clear that many of the critical methods for measuring these endpoints were in fact the same. "Ophthalmic safety" was to be determined by reviewing abnormal laboratory data and conducting an ocular examination of (a) ocular inflammation; (b) intraocular pressure; (c) ***visual acuity***; and (d) ***retinal bleeding***. *See* Ex. D, Trial Overview at 15. Ophthalmic safety was assessed by using biomicroscopy, indirect ophthalmoscopy, ***SD OCT***, CFP, and ***FA***. *See* ¶167. The secondary endpoint was to determine whether patients treated with AVA-101 required rescue injections by measuring (a) ***visual acuity***; (b) retinal thickness using ***SD-OCT***; and (c) leakage using ***FA***. *See* ¶¶168-175. Accordingly, reviewing the "safety data" for the AVA-101 Trial, specifically, visual acuity and retinal bleeding and SD-OCT and FA images, would necessarily constitute a review of the efficacy data because those same measures were used to determine efficacy, *i.e.* when rescue injections were required. The following chart shows the overlap in the measurements for the primary and secondary endpoints:

Endpoint Measures	Primary—Safety	Secondary—Efficacy
Biomicroscopy	✓	
Indirect Ophthalmoscopy	✓	
Retinal Thickness (SD OCT)	✓	✓
CFP	✓	

CNV Leakage (FA)	✓	✓
Visual Acuity	✓	✓
Ocular Inflammation	✓	
Intraocular Pressure (IOP)	✓	
Retinal Bleeding	✓	
Rescue Injections[23]	✓	✓

177. The standard therapy was given on day 0 and week 4. The subretinal injection was given to the treatment arm on week 1, and beginning with week 8, study visits were to occur every 4 weeks for 52 weeks for both the treatment arm and the control arm, totaling 12 visits. *See* Ex. C, Lancet at 2396. At each visit, patients were permitted to receive rescue injections according to a prespecified criteria based on BCVA, SD-OCT, and FA. Laboratory tests were also conducted. *See id.* The chart below was submitted with the Application Background and Research Plan for the AVA-101 Trial submitted to the TGA. The chart does not include every Trial visit; however, it shows the assessments that were conducted at each Trial visit:[24]

[23] As explained in ¶¶175-176 a review of visual acuity, SD OCT, and FA, the three measures used for the efficacy endpoint, which are also measures for the safety endpoint, would indicate the number of rescue injections required.

[24] While the source document does not provide a definition for the acronyms "SCR" and "BSL" used in the chart, counsel assumes those stand for "screening" and "baseline" assessments.

Table 1: Schedule of Assessments for AAV.sFlt-1 Injection

Procedures /Assessment	Week	SCR	BSL			1	2	4	8	12	16	24or early exit	36	52/ 78/ 156
	Visit	1	2	3	4	5	6	7	8	9	10	11	12	13
	day	-14 to -1	1	+1 day	+4 days	+7 days	14	30	60	90	120	180	210	360
Informed Consent , inclusion/exclusion criteria		X												
Medical /ophthalmic history		X												
Demography[1]		X												
Physical Examination		X												
Vital Signs (temperature, blood pressure & pulse rate)		X	X	X	X	X	X	X	X	X	X	X	X	X
ECG		X				X			X			X		X
BCVA by ETDRS		X	X		X	X	X	X	X	X	X	X	X	X
Biomicroscopic examination		X[2]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]	X[2]
IOP		X[2]	X	X[3]	X[3]	X[3]	X[3]	X	X	X	X	X[2]	X[2]	X[2]
Indirect ophthalmic examination		X[2]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]	X[2]
OCT		X[2]	X[3]					X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]
Colour fundus photos		X[2]						X[3]	X[3]	X[3]	X[3]	X[3]	X[2]	X[2]
Fluorescein Angiogram		X[3]						X[3]	X[3]	X[3]		X[3]	X[2]	X[2]
Laboratory tests[4]		X		X	X	X	X	X		X		X	X	X
Urinalysis		X		X	X			X		X		X	X	X
Therapeutic Drug Monitoring – PK[5]		X		X			X	X	X	X	X	X	X	X
Anti-VEGF ITV Injection[5]			X					X	(X)	(X)	(X)	(X)	(X)	(X)
Hospital Admission			X											
AAV.sFlt-1 Injection			X											
Concomitant medications		X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events[6]			X	X	X	X	X	X	X	X	X	X	X	X

AE = Adverse event; ECG = Electrocardiogram; BCVA = Best Corrected Visual Acuity;
ETDRS = Early treatment diabetic retinopathy study; IOP = Intraocular pressure;
OCT= Optical coherence tomography. Visit schedules may deviate.

1. Height and weight should be measured at the screening visit
2. Assessment performed in both eyes
3. Assessment performed in study eye only
4. Laboratory tests include: haematology (haemoglobin, platelets, WBC & differential); renal function (serum and blood urea nitrogen); hepatic function (serum bilirubin, alkaline phosphatase, GGT, SGOT/AST and SGPT/ALT); electrolytes (sodium, potassium, chloride, bicarbonate, calcium, phosphate). T-cell response will also be monitored. **At these time points tears, blood, urine and saliva samples will also be collected and analysed for AAV.sFlt-1 by real-time PCR, for presence of AAV capsid by ELISA and for changes in sFlt-1protein concentration by ELISA as proposed in this application.*
5. (X) means treatment provided only if required
6. AEs, after the first administration of study drug, should be recorded from the time of signing the informed consent form until the patient completes the study. If a subject withdraws, AE should be recorded until withdrawal or 30 days after the last dose of study drug, whichever is later.

178. The Trial Overview provides that in the AVA-101 Trial the primary safety endpoint data would be reviewed one month after injection and at additional intervals thereafter during the extended follow-up period. *See* Ex. D, Trial Overview at 2-3. The patients would remain on-study for 52 weeks, at which point there would be an additional data analysis. *See* Ex. H, April 2014 Abstract. Then, after that period of time, the Company would schedule two follow-ups at 18 months and 36-months after the first injection at which time the safety analysis for the primary endpoint was conducted. *See* Samuel B. Barone, CMO, Avalanche Biotechnologies, Inc., AVA-101 Phase 2a Study Results Call, 3 (June 15, 2015) (transcript on file with Bloomberg, Inc.).

C. Safety Monitoring for the AVA-101 Trial

1. Monitoring Safety Surveillance Data

179. When conducting a clinical trial the TGA provides that "[t]he sponsor is responsible for the ongoing safety evaluation of the investigational product(s)" and must conduct an "ongoing review and analysis of all information that is pertinent to the safety or benefit-risk assessment of the product." *See* Therapeutic Goods Administration, Note for Guidance on Good Clinical Practice, §5.16.1 (2000) ("**TGA GCP Guide**"); Therapeutic Goods Administration, Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines, §2.3.2 (2014) ("**TGA Pharmacovigilance Requirements**"). The FDA requires that "[t]he sponsor must promptly review all information relevant to the safety of the drug obtained or otherwise received by the sponsor from foreign or domestic sources" (21 C.F.R. § 312.32(b)) and "[t]he sponsor shall review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator (21 C.F.R. § 312.56(c))."[25]

180. "Safety analysis entails continuous surveillance of many variables with many subclassifications in the effort to look for signals of risk." Jay Herson, Data and Safety Monitoring Committees in Clinical Trials 48 (Shein-Chung Chow et al. eds. 2009). "Adequate surveillance

[25] While the AVA-101 Trial was registered with the TGA and thus subject to Australian regulations, Avalanche intended to seek approval of AVA-101 from the FDA and approval requires that testing of the drug complied with FDA regulations. *See* 2014 Form 10-K at 25.

requires integration of safety data from multiple sources, across multiple trials and even multiple indications during clinical development in order to characterize the developing safety profile." Laura McKain, M.D. et al., *Optimizing Safety Surveillance During Clinical Trials Using Data Visualization Tools*, Drug Discovery & Development (Oct. 6, 2015, 10:23 AM), http://www.dddmag.com/article/2015/10/optimizingsafetysurveillanceduringclinicaltrialsusingdatavisualizationtools ("Pharmaceutical companies must continuously monitor the safety of investigational products in development for adverse events that may be unexpected, occur at an increased frequency or severity, or result in an unexpected outcome. Ongoing safety signal detection leads to optimal patient protection and is essential to obtaining regulatory approval.") ("**Safety Surveillance Article**"). Thus, the FDA dictates that a sponsor should set up a systematic approach for safety surveillance that includes "a process for reviewing, evaluating, and managing accumulating safety data from the entire clinical trial database at appropriate intervals." *See* U.S. Food and Drug Administration, Guidance for Industry and Investigators: Safety Reporting Requirements for INDS and BA/BE Studies, at 13 (2012) ("**FDA Safety Reporting Guide**"). This requires establishing a central safety database where the safety data can be compiled and organized for review. *See* Safety Surveillance Article at 2.

181. During the course of conducting safety surveillance, the TGA provides that "[t]he sponsor should promptly notify all concerned investigator(s)/institution(s) and the regulatory authority(ies) of findings that could affect adversely the safety of the subjects, impact the conduct of the trial, or alter the IRB/IEC's approval/favourable opinion to continue the trial." TGA GCP Guidance, §5.16.2.

182. Thus, all of the safety assessments indicated in the chart in ¶177 *supra* recorded at each patient visit would have been compiled and analyzed on an ongoing basis for safety signals and risks as part of the trial's safety surveillance program. Constable was responsible for overseeing the collection of the data; Rakoczy and Lai were responsible for managing the data that had been generated. *See* ¶163.

2. Data Monitoring Committees

183. A data-monitoring committee ("**DMC**") "may be established by the sponsor to" review the accumulating safety surveillance data and "assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial." TGA GCP Guide §1.25. "In some cases, a specific independent committee with substantial external representation could be created to perform this function. In others, the sponsor may choose to create a safety team within the sponsor's organization." FDA Safety Reporting Guide at 13. "In either case, this independent group would oversee the evolving safety profile of the investigational drug and evaluate, at appropriate intervals, the accumulating data from individual and multiple clinical trials, as well as other available information." *Id.*

184. "A fundamental reason to establish a DMC is to enhance the safety of trial participants in situations in which safety concerns may be unusually high, in order that regular interim analyses of the accumulating data are performed." U.S. Food and Drug Administration, Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees, §2.1 (2006) ("**FDA DMC Guidance**"). The FDA recommends assembling a DMC in certain circumstances, including when "[t]here are *a priori* reasons for a particular safety concern, as, for example, if the procedure for administering the treatment is particularly invasive[.]" *Id.*

185. In order to evaluate the accumulating data in the trial, "[t]he study protocol will generally describe the schedule of interim analyses to be considered by the DMC, or the considerations that will determine the timing of meetings (e.g., a plan for interim analysis after a certain number of primary outcomes have been reported)." *Id.* at §4.3.1.1. An interim analysis reviews all of the safety and/or efficacy data accrued to date in order to compare treatment arms. *See* International Conference on Harmonization (ICH) guidance, E9 Statistical Principles for Clinical Trials, §4.2 (1998) ("**ICH E9 Guidance**") (Interim analysis "is any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to formal completion of

the trial[.]").[26] Thus, "[i]nterim analysis requires unblinded . . . access to treatment group assignment (actual treatment assignment or identification of group assignment) and comparative treatment group summary information." *Id.* "The study protocol will also typically describe the statistical approach to the interim analysis of trial data." FDA DMC Guidance §4.3.1.1.

186. In conducting the interim analysis, DMC typically receives an "interim report . . . that includes comparative effectiveness and safety data presented by study group[.]" *Id.* at §4.2.2. While the interim reports are often only reviewed by the DMC, "[i]n some cases (for example, ***in open-label trials with special concerns about safety***), there may be a rationale for the sponsor and/or investigators to have access to the ongoing comparative safety data to ensure continuous monitoring[.]" *Id.* at §4.2.2. As well, "the review of interim comparative data may raise certain questions that the DMC might want to address to the sponsor. These interactions may improve the quality of the monitoring process and may also provide the sponsor with information relevant to the costs, timetable, and likely interpretability of the study that can be of significant value in planning future studies and/or other aspects of product development." *Id.* at §6.2; ICH E9 Guidance at §4.5 ("[I]t is recognised that drug development plans involve the need for sponsor access to comparative treatment data for a variety of reasons, such as planning other trials.").

187. Another "fundamental responsibility of a DMC is to make recommendations to the sponsor . . . concerning the continuation of the study. Most frequently, a DMC's recommendation after an interim review is for the study to continue as designed." *Id.* at §4.4.3.1. "Other recommendations that might be made include study termination, study continuation with major or minor modifications, or temporary suspension of enrollment and/or study intervention until some uncertainty is resolved." *Id.*

[26] Both the FDA and the TGA have adopted these ICH guidelines. *See E9 Statistical Principles for Clinical Trials*, ICH, http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/statistical-principles-for-clinical-trials.html (last visited Nov. 16, 2016); *Clinical and Safety Guidelines*, TGA, https://www.tga.gov.au/clinical-efficacy-and-safety-guidelines (last visited Nov. 16, 2016).

188. For the AVA-101 Trial "[s]tudy data and adverse events were monitored by a data safety monitoring committee with expertise in retinal diseases and gene therapy vectors." Ex. C, Lancet at 2398. The DMC and Avalanche reviewed interim safety surveillance data in June 2014. *See* 2014 Form 10-K at 1. Indeed, Avalanche explained to analysts that "[t]he trial included an interim safety analysis which was conducted in June of 2014" which revealed no issues. Phil Nadeau, Cowen & Co., *Highlights from Lunch with Management*, 1 (2015); *see also* Joshua Schimmer, Piper Jaffray, *Avalanche Biotechnologies (AAVL), On the Road With Management; Increasing PT*, 1 (2014) (after hosting Avalanche for meetings stated "AAVL remains on track to report topline data in the middle of 2015, following a prior interim safety look that revealed no safety concerns.").

3. Pharmacovigilance Committees

189. In addition to setting up a DMC to review ongoing safety surveillance data, a sponsor should have a pharmacovigilance group within the company to handle adverse event reporting. *See* Herson, Data and Safety Monitoring, at 49. Pharmacovigilance means all scientific and data gathering activities relating to the detection, assessment, and understanding of adverse events ("**AE**") or adverse reactions ("**AR**").[27] *See* Therapeutic Goods Administration, Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines, 7 (2014) ("**TGA Pharmacovigilance Requirements**"); U.S. Food and Drug Administration, Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, 4 (2005) ("**FDA Pharmacovigilance Guidance**"). The purpose of this committee is to ensure that information about all ARs detected during the clinical trial that are "reported to the sponsor or people who work for the sponsor . . . is collected, collated,

[27] The TGA defines an Adverse Event as "[a]ny untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment." *See* TGA GCP Guidance at 6. An Adverse Reaction is defined as "all noxious and unintended responses to a medicinal product related to any dose" meaning that "a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility[.]" *Id.*

and held so that it may be accessed" and to "coordinate the preparation of AR reports[.]" Therapeutic Goods Administration, Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines, §1.2.2 (2014) ("TGA Pharmacovigilance Requirements"). The TGA advises that "[t]he pharmacovigilance system should be developed to allow acquisition of sufficient information for the scientific evaluation of AR reports and any other safety issues associated with the medicine." *Id.*

190. The reason a sponsor needs a pharmacovigilance committee is that throughout the course of a clinical trial in Australia, a sponsor must report to the TGA (1) "all serious unexpected and serious expected ARs . . . that become known to the sponsor, and are associated with the use of the medicine or active substance in the medicine;"[28] (2) "significant safety issues identified by the sponsor as a result of its ongoing review and analysis of all information that is pertinent to the safety or benefit-risk assessment of the product"; (3) all clinical and medically relevant information in relation to serious ARs occurring in Australia that becomes available to the sponsor as a result of follow-up activities: and" (4) "a suspected increase in the frequency of serious ARs to the medicine, including the basis on which the frequency assessment has been made." TGA Pharmacovigilance Requirements at §2.3.1. All serious ARs must be reported to the TGA no later than 15 days after they are made known to the sponsor and all significant safety issues must be reported within 72 hours. *See id.* at §2.4.1.

191. The FDA also requires that a sponsor promptly review and report adverse events. *See* FDA DMC Guidance §4.4.1.2 (citing 21 CFR 312.32(b); 21 CFR 812.42(d); 21 CFR 812.46(b)).

192. The AVA-101 Trial "has a pharmacovigilance committee which monitors adverse events" and "Avalanche would be informed of any serious complications made known to the

[28] The TGA defines an Unexpected Adverse Reaction as an adverse reaction, the nature or severity of which is not consistent with the applicable product information (*e.g.*, Investigator's Brochure for an unapproved investigational product). *See* TGA GCP Guidance at 13.

pharmacovigilance committee[.]" Phil Nadeau, Cowen & Co., *Highlights from Lunch with Management*, 2 (Mar. 5, 2015).

193. Accordingly, pursuant to federal regulations and the Trial procedures, Avalanche, as a sponsor of the Trial, was receiving adverse event reports on an ongoing basis throughout the AVA-101 Trial.

D. Progression of Phase 1 of the AVA-101 Trial

194. Phase 1 of the AVA-101 Trial began in January 2012, and by April 2012 all 8 patients had been enrolled. Pursuant to the Trial Overview, the one-month primary endpoint (safety) data for the 8 patients was gathered. *See* Ex. D, Trial Overview at 2-3. As part of the extended follow-up permitted by the trial protocol, an 8-week safety evaluation analysis was conducted for these patients. The results of this 8-week evaluation were reported at the meeting of the American Society for Cell and Gene Therapy held in May 2012. *See* Ex. E, 2012 LEI Annual Report; Ex. C, Lancet at 2396. The meeting abstract published on May 3, 2012 stated that "***[a]t day 60 none of the patients required rescue treatment***. ***There was no evidence of visual acuity loss***, IOP elevation,[29] ***retinal detachment***,[30] or any intraocular or systemic immune response in any of the patients." Ex. G, May 2012 Abstract. This abstract indicates that the safety/efficacy endpoint measures were evaluated at week 8. ***Rakoczy explained that this 8-week marker was significant as "this period of time provided an adequate window to allow time for the start of sFLT-1 protein expression" to develop from the AVA-101 injection***. Ex. C, Lancet at 2396. Indeed, the fact that the 8-week results were reported to the medical community demonstrates conclusively that 8-week results are material.

195. Beginning in April 2012 Avalanche began enrolling patients in Phase 2a of the AVA-101 Trial. *See* 2014 Registration Statement at 2.

196. By the end of 2012, 12 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Ex. E, LEI 2012 Annual Report at 20.

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[29] "**IOP**" is an acronym for intraocular pressure.

[30] Retinal detachment is detected using SD OCT.

197. In May 2013, Rakoczy, Chalberg, Blumenkranz, and Constable, along with others, published an abstract with a 10-month "Progress Report" to "assess the safety, pharmacology, and immunology of rAAV.sFlt-1 gene therapy" and disclosed that "5 out of 6 patients treated with gene therapy did not require reinjection over the study period whereas 2/2 controls met re-treatment criteria." Ex. I, May 2013 Abstract.

198. In June 2013, Avalanche and LEI published an abstract prepared by Chalberg and Blumenkranz, among others, in the Investigative Ophthalmology & Visual Science ("**IOVS**") journal discussing the safety of subretinal injections for ***the first 17 patients*** enrolled in the AVA-101 Trial, ***which necessarily included 9 patients enrolled in Phase 2a of the Trial***. *See* Ex. K, June 2013 Abstract. The abstract noted that "[t]he induced bleb[31] was transient, able to be visualized clinically and ***via optical coherence tomography (OCT)*** at 2 hours, but invisible by 24 hours post injection[]" and "[d]elivery was successfully documented in all 12 subjects." *Id.*

199. The May 2012, May 2013, and June 2013 abstracts reported interim results that were gathered and analyzed as part of the extended follow-up permitted by the Trial's protocol. *See* Ex. D, Trial Overview at 2-3; ¶178 *supra*. These reports indicate that LEI and Avalanche were taking advantage of the status of the AVA-101 Trial as open-label, and were periodically dipping in to review data on an ad hoc basis. As well, in its 2012 Annual Report, LEI stated that "[t]o date, all patients are doing well and we are looking forward to further data analysis in 2013[.]" Ex. E, LEI 2012 Annual Report at 20. The report also explained that by the end of the year the 30th of 32 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See id.*

200. By no later than February 8, 2014, all 32 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Ex. J, Retina Today Article.

[31] A "bleb" is a fluid-filled bubble or blister that can form on the retina of the eye. *See Trabeculectomy (Filtration Surgery) for Glaucoma*, WebMD, http://www.webmd.com/eye-health/trabeculectomy-filtration-surgery-for-glaucoma (last visited Dec. 1, 2016).

E. Avalanche's Plan To Take the Company Public

1. Announcement of the Phase 1 Results

201. In the several months leading up to Avalanche's IPO in July 2014, The Exchange Act Defendants rolled out part one of their plan to reap millions of dollars by taking the company public. In order to ensure that Avalanche would be offered up at the highest price, LEI and Avalanche began to garner the industry's enthusiasm over Avalanche and its Ocular BioFactory™ platform by announcing and aggressively promoting the remarkable results from Phase 1 of the AVA-101 Trial.

202. For example, in April 2014, Avalanche and LEI published an abstract prepared by Chalberg, Blumenkranz, and Schwartz, among others, in the IOVS journal touting the one-year results from the first phase of the AVA-101 Trial (the April 2014 Abstract). *See* Ex. H, April 2014 Abstract. The timing of this announcement was suspect because this data was available an entire year earlier when Phase 1 of the Trial met its one-year mark in April 2013. *See id.*

203. The April 2014 Abstract touted the large gain in visual acuity, decrease in retinal thickness, and virtual absence of rescue injections in the treated group:

> ***There was no evidence of loss of visual acuity***, intraocular pressure elevation, retinal detachment, or intraocular or systematic inflammation in any patients in the last study visit. . . .
>
> ***SD OCT demonstrated the decrease or lack of fluid in the retina of all patients. Average center point thickness was 552 + 132 um at baseline and decreased to 352 + 68 um at 1 year***. . . .
>
> ***The average visual acuity was 41.8 EDTRS letters at baseline, which increased to 49.3 letters at one year***. . . .
>
> During the one year follow up period, subjects were allowed retreatment with ranibizumab according to strict, masked re-treatment criteria; ***out of a possible 72 injections, 2 rescue injections were given. Control subjects received 10X as many retreatments during the criteria-driven PRN period***. . . .
>
> These results suggest that subretinal rAAV.sFlt-1 injection is safe, and well tolerated by the elderly study population, and that ***previous or concurrent ranibizumab injections do not interfere with safety***.

See id.[32]

204. Specifically, the results showed that in Phase 1, AVA-101 had the desired effect in the treatment arm as on average retinal thickness ***decreased by 200 um***, ***visual acuity increased by 7.5 letters***, and ***5 of 6 patients in the treatment arm received 0 rescue injections***, meaning that out of a possible 72 rescue injections, ***only 2 rescue injections were given (both to the same patient)***. Control subjects received ten times more rescue injections than patients in the treatment arm. *See* Ex. H, April 2014 Abstract; Ex. I, Elizabeth P. Rakoczy, et al., *Gene Therapy for Wet-AMD: Progress Report on Phase I/II Clinical Trial*, 21 Molecular Therapy S22 (2013).

205. Also in April 2014, Retina Today published an article quoting Chalberg's presentation of the results at the Angiogenesis, Exudation, and Degeneration 2014 Conference held on February 8, 2014. *See* Ex. J, Retina Today Article. Quoting Chalberg, the article stated: "***[o]cular gene therapy might be a long-term viable option for patients with Wet AMD***" and repeated much of the positive data from the April 2014 Abstract:

> The control group, which did not receive an injection of AVA-101, required a mean 3 injections of ranibizumab during the 12-month period.
>
> ***The treatment group required a mean 0.3 ranibizumab injections over the same period***. . . .
>
> Patients received ranibizumab injections if fluid appeared on OCT or fluorescein angiography, or if there was vision loss attributable to increased area of choroidal neovascularization. . . .
>
> "Because these patients are coming heavily pretreated, we didn't necessarily expect them to gain additional vision," Dr. Chalberg said. "***But treated patients actually gained between 9 and 12 letters over 12 months***."

206. On May 5, 2014, LEI and Avalanche again presented the April 2014 Abstract boasting a positive anti-VEGF response from Phase 1 of the AVA-101 Trial at the annual meeting of the Association for Research in Vision and Ophthalmology, Inc. ("**ARVO**").

[32] A careful read of the April 2014 Abstract shows that the efficacy data and safety data are often conflated as they are collected through the same data measures.

207. Shortly thereafter, on May 19, 2014, LEI published a media statement entitled "New Gene Therapy Could Bring Relief for Eye Disease Patients" in which LEI expressed its excitement over the interim data from the AVA-101 Trial and declared that the results "***could spell the end of invasive monthly injections into the eye[.]***" The media statement also disclosed the following:

> Principal clinical investigator Professor Ian Constable and the LEI clinical team have recruited 40 patients to the trial. Professor Constable said the ***gene therapy was proving well tolerated and promising in human trials currently under way***.
>
> Early results on safety and efficacy from the first eight patients in the trial were reported to the Association for Research in Vision and Ophthalmology (ARVO) annual conference in Florida earlier this month by principle scientific investigator Winthrop Professor Elizabeth Rakoczy.
>
> "***To date, the safety profile is excellent – we have found no serious adverse effects in the eye – and so far we have promising data on how it works***," Professor Constable said.

208. LEI also published a Spring Newsletter that contained the same content as the May 19, 2014 media release. *See* Lions Eye Institute, Spring Newsletter, 3 (2014).

209. These announcements all followed the same theme: one subretinal injection of AVA-101 may cure Wet AMD because the results from Phase 1 of the AVA-101 Trial showed that all but one patient was able to maintain stable vision without the need for a rescue injection for an entire year. As one analyst noted, "the proof-of-concept results are ***impressive with a functional cure*** in patients" treated in Phase 1 of the AVA-101 Trial. Tim Lugo, William Blair, *ARVO Wrap-Up: Gene Therapies Continue to Look Impressive Ahead of 2015 Data Sets*, 2 (2015).

210. In the midst of this excitement, in June 2014 Avalanche received the "[i]nterim drug safety surveillance data" from the AVA-101 Trial which suggested that "AVA-101 continues to be well tolerated[.]" 2014 Registration Statement at 2. This interim data was presumably provided to Avalanche in the same data report given to the DMC to conduct an interim safety analysis for the AVA-101 Trial. *See* ¶188 *supra*. Despite the fact that since 2012 Avalanche and LEI had consistently announced details concerning the positive interim data from the AVA-101 Trial, none of this interim data was disclosed to the public. This time, the Exchange Act Defendants only indicated which adverse events were observed:

> Adverse events related to study procedures include ***subconjunctival, vitreous and retinal hemorrhage, cataract progression*** and eye pain. Other infrequent adverse events may be related to study procedures, including ***retinal tears or holes*** and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss.

211. At this time, in June 2014, the safety surveillance data, which included all of the measures set forth in the chart in ¶177 *supra*, would have contained a significant amount of safety/efficacy data for each patient. By the end of 2012, 12 patients had been enrolled in Phase 2a of the AVA-101 Trial, meaning that the full 1-year data was available for the first 12 of 32 patients enrolled in Phase 2a by December 2013. *See* Ex. E, LEI 2012 Annual Report at 20. By the end of 2013, 30 of 32 patients had been enrolled in Phase 2a of the AVA-101 Trial. *See* Lions Eye Institute, Annual Report, 31, 35 (2013). Thus, if patients enrolled steadily throughout the year of 2013, full 1-year data would have most likely been available for 21 of 32 patients by June 2014 (the 21 patient tally was calculated by adding the 12 patients enrolled in 2012 to 9 patients, or half of the additional 18 patients enrolled in 2013), and longer than 6-month data would have been available for the remaining 9 patients enrolled in the latter half of 2013. In any event, by February 8, 2014, all 32 patients had been enrolled in Phase 2a the AVA-101 Trial (¶200), meaning that by June 2014, at least 4-month data was available for all patients. Even in the highly unlikely event that all 18 additional patients who enrolled in 2013 did so at the last possible moment in December 2013, the June 2014 data would include 1-year data for 12 patients, 6-month data for 18 patients, and at least 4-month data for the 2 patients who enrolled in 2014. *See* Ex. J, Retina Today Article. Lastly, this data would have also contained the 8-week safety review for every single patient in Phase 2a that was conducted in Phase 1 and would have been conducted in Phase 2 as part of the DMC's obligation to conduct interim analyses of the safety data. ¶194.

212. Furthermore, even review of the adverse event reports at this time would have indicated safety/efficacy data for those patients. Vitreous or retinal hemorrhage is detected and analyzed by using SD OCT. *See Vitreous Hemorrhage*, Retina Eye Specialists, http://www.retinaeye.com/vitreoushemorrhage.html (last visited Nov. 10, 2016). Retinal holes are

also diagnosed using SD OCT. *See Macular Hole Diagnosis*, American Academy of Ophthalmology, http://www.aao.org/eye-health/diseases/macular-hole-diagnosis (last visited Nov. 9, 2016). Cataracts are detected using a visual acuity test. *See Facts About Cataract*, National Eye Institute, https://nei.nih.gov/health/cataract/cataract_facts (last visited Nov. 9, 2016). Also, in addition to the tests relating directly to the adverse events, adverse event reports include sufficient medical records for each patient to identify the potential sources and the resolution of the adverse event. *See, e.g.*, Therapeutic Goods Administration, *Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting*, Attachment 1 (2000). Thus, the safety/efficacy data gathered for each patient experiencing an adverse event would have been included in these adverse event reports. Although, it would have been nonsensical for Avalanche to have received an interim safety anaylsis of just adverse event reports considering that the Company was supposed to be receiving them on an ongoing basis as the Trial progressed.

213. On July 15, 2014, Ophthalmology Times published an article—reviewed by Rakoczy—discussing the "[p]reliminary encouraging data on long-term gene therapy for exudative age-related macular degeneration" from Phase 1 of the AVA-101 Trial. *See* Nancy Groves, *Long-term gene therapy for wet AMD promising: One year follow-up on rAAV.sFt-1 finds no evidence of inflammation, IOP elevation, events, clinical changes*, Ophthalmology Times, July 15, 2014. In regard to the design of the trial, the article quoted Dr. Rakoczy stating, "'[w]e wanted to make sure that during that time they were protected against the harmful effects of neovascularization in the eye' . . . After that, ranibizumab was provided only as rescue therapy." *See id.*

214. In regard to the results, the article reiterated that safety was excellent, that retinal thickness decreased, patients gained visual acuity, and patients required nearly no rescue injections. Specifically, the article stated, "***[t]he safety is excellent, and we have seen longterm benefits for the patients from this approach*** . . . ***Patients who receive our treatment do not need any retreatments, or very few, and the growth of new blood vessels in the eye can be controlled without any additional intervention***. . . . In all, ***5 of the 6 treated subjects gained vision***. . . ."

2. The IPO and the 2015 Offering

215. The second part of the Exchange Act Defendants' plan was to monetize the positive results from the first 8 patients from the AVA-101 Trial. Indeed, Avalanche took full advantage of the growing excitement over the favorable Phase 1 results of the AVA-101 Trial and on May 30, 2014 launched its IPO by filing a registration statement with the SEC on Form S-1 (Registration No. 333-197133). Following amendment, on the first day of the Class Period, July 30, 2014, the SEC declared the registration statement effective. The IPO was priced at $17 per share. On July 31, 2014, the first day of the Class Period, Avalanche and the Individual Exchange Act Defendants filed the final prospectus for the IPO (the "**2014 Prospectus**"), which forms part of the registration statement (the 2014 Prospectus and registration statement are collectively referred to herein as the "**2014 Registration Statement**"), and sold 6,900,000 shares of common stock to the investing public. The IPO was completed on August 5, 2014 and Avalanche raised $106.8 million, after deducting underwriting discounts and commissions and estimated offering expenses. *See* Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (Aug. 5, 2014). The IPO provided for a lock-up period, whereby no directors or executive officers of Avalanche were permitted to sell their shares for 180 days from the date of the 2014 Prospectus, or until January 17, 2015. *See* 2014 Registration Statement at 44.

216. Avalanche's debut was met with an outstanding reception by the investment community. On July 31, 2014, the first trading day, Avalanche's stock price closed at $27.99, climbing nearly 40%, even after being priced above expectations. This reaction was primarily due to the data from Phase 1 of the AVA-101 Trial. Cowen & Company initiated coverage on August 25, 2014, attributing its Outperform rating and price target of $45 to the "promising early data that suggests [AVA-101] has the potential to be a functional cure for wet AMD." Phil Nadeau, Cowen & Co., *Initiation: One Stick in the Eye Is Better Than Many*, 1 (2014). William Blair initiated coverage the same day with an Outperform rating and what it considered a "likely conservative" price target of $52 based upon the data collected to date. Tim Lugo, William Blair, *Eyeing the Next Disruption in the AMD Market; Initiating Coverage With Outperform Rating and $52 Price Target*,

1 (2014). With a Buy rating and slightly lower price target of $40, Jefferies initiated coverage stating, "AAVL shares hold significant promise based on PI data with AVA-101 observing meaningful VA improvements and durable responses in wAMD patients, which supports a favorable outlook for the PIIa study expected in mid-'15." Biren Amin, Jefferies, *Initiate at Buy: AAVL Gene Therapy Has Disruptive Potential in Wet AMD*, 1 (2014).

217. For the remainder of 2014 Avalanche went out into the market and touted the safety and efficacy of AVA-101 as a treatment for Wet AMD. Indeed, Avalanche presented at least seven different medical and investment conferences over the course of four months. *See 2014 News Releases*, Avalanche Biotechnologies, Inc., http://investors.avalanchebiotech.com/phoenix.zhtml?c=253634&p=irol-news&nyo=2 (last visited Jan. 29, 2016). The Powerpoint presentation Avalanche made at many of the industry conferences contained broad assertions regarding AVA-101's efficacy including that ***"[o]ne-time, subretinal injection offers 'functional cure' of wet-AMD***" and "***[s]ubjects gained/maintained vision with no or minimal need for additional treatment over one year***." *See* ¶247 *infra*.

218. The hype generated by Avalanche and the Individual Exchange Act Defendants caused the Company's stock price to skyrocket to a high of $55.89 by the end of 2014. Avalanche and the Individual Exchange Act Defendants decided to take advantage of this record-high stock price and on December 18, 2014, Avalanche filed with the SEC its registration statement on Form S-1 (Registration No. 333-201388) for a secondary offering of common stock. Following amendment, on January 7, 2015 the registration statement was declared effective by the SEC and Avalanche, the Individual Exchange Act Defendants, and the underwriters priced the 2015 Offering at $59 per share (the "**2015 Offering**"). On January 7, 2015, Avalanche and the Exchange Act Defendants filed the final prospectus for the 2015 Offering (the "**2015 Prospectus**"), which forms part of the registration statement (the 2015 Prospectus and the registration statement are collectively referred to herein as the "**2015 Registration Statement**") with the SEC, and sold 2,399,457 shares of common stock, plus the underwriters' over-allotment of an additional 359,918 shares, to the investing public. On that day, Avalanche common stock reached its Class Period high, closing at

$60.08 per share. The 2015 Offering was completed on January 13, 2015 and Avalanche raised approximately $130.5 million, after deducting underwriting discounts and commissions and estimated offering expenses. *See* Avalanche Biotechnologies, Current Report (Form 8-K) (Jan. 13, 2015).

219. As part of this Offering, insiders took advantage of the one exception to the still-ongoing lock-up period from the IPO and sold a total of 290,000 shares of common stock for total proceeds of $16,083,400 in the 2015 Offering. *See* ¶¶153-168 *infra*. These sales constituted 10% of the entire offering. And when the lock-up period for the 2015 Offering expired two months prior to the date when the results from Phase 2a were ultimately announced, Avalanche insiders immediately began selling more than 350,000 shares of Avalanche common stock for total proceeds of $12,908,310. *See id.*

3. Progression of Phase 2a of the AVA-101 Trial

220. Mere days after the secondary offering, on January 16, 2015, Piper Jaffray published an analyst report summarizing its discussions with Avalanche management. The report stated, in relevant part, that "[m]anagement notes ***they do know or see the P2a data***, but are trying to contain expectations that the dramatic reduction in anti-VEGF antibody injection frequency in P1a may not be reproduced." Joshua E. Schimmer, Piper Jaffray, *Things We Learned This Week That You Might Not Know*, 1 (2015). Several hours later, Piper Jaffray issued a follow-up report to correct its alleged typo and instead wrote that "management notes ***they do NOT know or see the data***" for Phase 2a of the AVA-101 Trial, and further elaborated that "[t]he company is insistent that ***there is nothing they know about the trial which would change their views or expectations for the study***." Joshua E. Schimmer, Piper Jaffray, *Clarification on P2a AMD Data Expectation and Our Discussions With Management*, 1 (2015).

221. Despite Piper Jaffray and Avalanche's after-the-fact retraction, the market was not convinced, and on January 16, 2015, shares of Avalanche common stock dropped $3.19, or more than 6%, to close at $48.37 and never recovered above $50 again.

222. In fact, the Exchange Act Defendants had seen a significant amount of the efficacy-related data for Phase 2a of the AVA-101 Trial.[33]

223. First, based upon the periodic safety data reported during the course of Phase 1 (*i.e.*, the 8-week data reported in May 2012, the progress report in May 2013, and the 17 patient data reported in June 2013) the Trial protocol permitted interim review on an ad hoc basis of at least the safety data throughout the course of the Trial. ***Indeed, some time before June 2013 Avalanche, Chalberg, and Blumenkranz viewed the safety data for 9 patients in Phase 2a and published an analysis in an abstract in the IOVS journal regarding the results***. *See* Ex. K, June 2013 Abstract.

224. As part of the interim analysis of the safety data permitted by the DMC per the Trial protocol, the same 4-week and 8-week safety analyses that were conducted for patients enrolled in Phase 1 of the Trial pursuant to the Trial protocol was also presumably conducted for patients enrolled in Phase 2a of the Trial. *See* ¶¶194, 211. Because the Trial was fully enrolled by February 8, 2014, by April 8, 2014, each patient in Phase 2a was past week 8 of treatment and thus the 8-week interim analysis could be performed. After the Class Period, Avalanche noted that within the first 8 weeks of treating patients in Phase 2a, data showed that retinas were thickening for patients in the treatment arm and thinning for patients in the control arm by a difference of 81 um—the opposite of what you would see with an effective drug—and this delta remained constant throughout the Trial. *See* Salveen Richter, SunTrust Robinson Humphrey, *Await Further AVA-101 Clarity, Lack of Near-Term Catalysts, DGrading to Neutral*, 1 (2015). Thus, the trend of retinas thickening in the treatment group and thinning in the control group would have been visible in the safety data for all Phase 2a patients at least in the interim 8-week analyses. This 8-week analysis

[33] On March 25, 2015, at Avalanche's Analyst and Investor Day Conference, when asked what he would like to see in the Phase 2a top-line results, Jeffrey Heier, a consulting ophthalmologist working with Avalanche on the AVA-101 Trial, stated "I think safety, obviously, we always look for safety. ***We want to see the continued tolerability in safety we've seen from the Phase 1, and what we've seen from 2a***." Webcast: *Avalanche Biotechnologies Analyst and Investor Day*, Avalanche Biotechnologies (Mar. 25, 2015) http://investors.avalanchebiotech.com/phoenix.zhtml?c=253634&p=irol-EventDetails&EventId=5183324.

would have also showed that a material number of patients in the treatment arm were requiring rescue injections.

225. In June 2014, Avalanche "received" "***[i]nterim drug safety surveillance data [] in June 2014 from this ongoing study."*** 2014 Registration Statement at 2. Given the DMC's obligation to conduct ongoing interim review of the safety data in the AVA-101 Trial, this interim analysis would have contained a significant amount of safety/efficacy data for each patient. Specifically, at this time, the safety surveillance data would have likely contained full 1-year data for 21 of 32 patients, 6-month or greater data for 9 patients, and at least 4-month data for the remaining 2 patients enrolled in Phase 2a of the Trial. At the very least, this data would have contained the 8-week safety review for every single patient in Phase 2a of the Trial.

226. Thus, the 2014 interim safety surveillance data would have contained a sufficient amount of patient safety/efficacy data to indicate that retinas were thickening in the treatment group and that patients in the treatment group were receiving rescue injections at a materially higher rate than those in Phase 1 of the AVA-101 Trial.

227. Further, if the June 2014 interim analysis of the safety surveillance data that the DMC provided to the Company somehow did not include all of the ocular safety measures from Phase 2a of the Trial up to that date, the Exchange Act Defendants were deliberately reckless in failing to obtain that information from the DMC. Instead, they chose to obscure the correlation between the safety data and the efficacy data and only discuss adverse event reports to conceal the fact that this interim safety surveillance data indicated that AVA-101 was not having the desired effect in patients enrolled in Phase 2a.

228. For that matter, even if the interim safety surveillance data only contained adverse event reports (which it by definition did not), Defendants still would have been aware that AVA-101 was not having the desired effect in patients enrolled in the Phase 2a Trial. Indeed, a review of the adverse event reports generated as of June 2014 would have included many of the safety/efficacy measures, *e.g.*, OCT and visual acuity, that would have indicated that AVA-101 was not effective in those patients. ¶212.

229. In addition to these established facts demonstrating that the Exchange Act Defendants were in possession of adverse interim safety/efficacy data for Phase 2a of the AVA-101 Trial during the Class Period, the Exchange Act Defendants' attempts to "reel back" enthusiasm for the Phase 2a results further supports this inference.

230. That is, after the IPO ***and the 2015 Offering***, as observed by Piper Jaffray in its original January 16, 2015 analyst report, "[t]he company is focused on 'managing expectations' for the 1H15 P2a data for AVA-101 in Wet AMD and focusing on an emerging pipeline which it will highlight at its analyst event in March." Joshua E. Schimmer, Piper Jaffray, *Things We Learned This Week That you Might Not Know*, 1 (2015). Furthermore, in an e-mail interview given by Chalberg and Blumenkranz to Lowenthal Capital Partners on May 22, 2015, Avalanche greatly changed its tune from that prior to the IPO and reiterated several times that the AVA-101 Trial "is a safety study, so [the] primary goal is to ensure that there are no major safety issues. The study is not powered for statistical significance of secondary endpoints." Interview with Dr. Thomas Chalberg, CEO, and Dr. Mark Blumenkranz, Chairman of the Board, Avalanche Biopharmaceuticals, Inc., *via* e-mail (May 22, 2015), *available at* http://seekingalpha.com/article/3205796-avalanche-management-addresses-wall-streets-concerns-ahead-of-binary-catalyst. The need to "manage expectations" and refocus attention on the safety outcome measures further demonstrates that the Exchange Act Defendants possessed negative efficacy results.

4. The Phase 2a Topline Results

231. As promised, on June 15, 2015, Avalanche released the top-line results from Phase 2a of the AVA-101 Trial. The Company announced the following:

> Phase 2a clinical study for AVA-101 met its 12-month primary endpoint, based on ophthalmic and systemic safety, demonstrating that AVA-101 was well tolerated with a favorable safety profile in subjects with wet age-related macular degeneration (wet AMD). . . .
>
> There were no unexpected administration-related adverse events, and any events that occurred resolved without visual sequelae. . . .

> ***Overall, BCVA mean change from baseline did show a significant difference of 11.5 letters between the treatment (+2.2 letters) and control (-9.3 letters) groups (95 percent CI, 2.3-20.7 letters)***.
>
> ***The median number of rescue injections using the protocol-specified retreatment regimen was 2 (95 percent CI, 1-6 injections) in AVA-101 treated subjects compared with 4 (95 percent CI, 3-5 injections) in the control group***. More subjects required fewer retreatments in the treatment group compared with control (19.0 percent vs. 9.1 percent with 0 injections; 33.3 percent vs. 9.1 percent with ≤1 injections; 52.4 percent vs. 9.1 percent with ≤2 injections).
>
> ***Retinal thickness mean change from baseline***, as reported by the site using automated segmentation, ***was +25 µm for AVA-101 treated subjects compared with -56 µm in the control group*** (CI for the difference, 17 to 145 µm).

232. Later that day, the Company held a special conference call and continued to carry out its deception by attempting to conceal the true implication of these results. For example, Chalberg tried to put a positive spin on the data by reiterating several times that "the key takeaway is that this was a positive Phase 2a study that met its primary objective which was to further establish the safety of AVA-101 in Wet AMD patients and also help inform future studies going forward. But in this very difficult-to-treat population, we're very encouraged to also see that AVA-101 showed promising signs of efficacy" and "[t]hese results demonstrate that AVA-101 could potentially benefit a significant portion of patients of wet AMD." Thomas W. Chalberg, CEO, Avalanche Biotechnologies, Inc., AVA-101 Phase 2a Study Results Call, 5 (June 15, 2015) (transcript on file with Bloomberg, Inc.).

233. In the end, the Exchange Act Defendants could not hide what the Company would later admit in November 2015, namely that the AVA-101 Trial "***did not [show] evidence of a complete and/or durable anti-VEGF response in the majority of subjects treated with AVA-101 as administered in the Phase 2a study***[.]" Avalanche Biotechnologies, Inc., Quarterly Report (Form 10-Q), 17 (Nov. 9, 2015). Indeed, retinal thickness, a critical anatomic efficacy measure, ***increased in patients treated with AVA-101 by 25 um*** whereas ***it decreased in the control group by 56 um***. *Id.* at 15. This means that AVA-101 was not only ineffective at inhibiting blood vessel growth and leakage in the retina because retinas increased instead of decreasing as intended, it fell far behind the current therapy. As a gene therapy, AVA-101 was designed to permanently change the cells in

the retina to combat VEGF, eliminating the need for another injection over the patient's lifetime. However, the results from the trial showed that AVA-101 treated subjects received "***a mean of 3.1 rescue injections***" compared with "***a mean of 3.6 rescue injections for subjects in the control group***." This near equivalent mean measurement occurred because 10 of the 21 patients who were treated with AVA-101 received ***between 3 and 7 rescue injections***, whereas 10 of the 11 patients treated in the control group needed ***between 3 and 5 rescue injections***. *See id.* Clearly the drug did not work as intended, and for some patients was less effective than the current therapy. Finally, the improvement in visual acuity as an improvement in only 2 letters was negligible. These results stand in stark contrast to the Phase 1 results showing a ***decrease in retinal thickness by 200 um***, an ***increase in visual acuity by 7.5 letters***, and ***5 of 6 patients needing 0 rescue injections***.

234. The market saw through the Exchange Act Defendants' smokescreen on the Phase 2a data and was not impressed by the results. In an article entitled "Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club," one commentator stated that "I'm struggling to adequately describe the awfulness of Avalanche Biotechnologies' [] performance Monday night[.]" The author pointed out that when investors looked deeper at the results, they realized the flaws, concluding that "the painful lesson here is that Avalanche's study of AVA-101 may have achieved its primary efficacy endpoint, but the gene therapy failed the more important common sense endpoint." Adam Feuerstein, *Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club*, The Street (June 16, 2015), http://www.thestreet.com/story/13187351/1/avalanchefailscommonsensetestkickedoutofgenetherapycredibilityclub.html. Zacks called the data "lackluster" and "weak" explaining that the "results disappointed investors[.]" *Avalanche Biotechnologies Slips on Weak AVA-101 Data*, Zacks Equity Research (June 16, 2015), http://www.zacks.com/stock/news/178460/avalanche-biotechnologies-slips-on-weak-ava101-data. An article published on investing website, the Motley Fool, explained that "[t]he problem is that the retinas of patients receiving AVA-101 thickened relative to those in the control group, casting doubt on the gene therapy's efficacy as a treatment for wet AMD[,]" "one would expect the *exact* opposite result if AVA-101 was truly helping patients maintain their visual

acuity." George Budwell, *Why Avalanche Biotechnologies, Inc. Stock Collapsed Today*, Motley Fool (June 16, 2015), http://www.fool.com/investing/general/2015/06/16/why-avalanche-biotechnologies-inc-stock-collapsed.aspx.

235. On this news shares of Avalanche common stock plummeted $21.83, or more than 56%, to close on June 16, 2015 at $17.05 per share.

236. On July 23, 2015, Avalanche announced that Chalberg would resign as CEO and president and as a member of the Board of Directors effective that day. *See* Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (July 23, 2015). He was, however, to remain as a consultant for Avalanche and member of the Scientific Advisory Board. *See id.*

F. The AVA-101 Trial Is Abandoned

237. Throughout the Class Period, Avalanche and the Individual Exchange Act Defendants represented that after announcing data from Phase 2a of the AVA-Trial in the middle of 2015, Avalanche would conduct Phase 2b of the AVA-101 Trial "in the second half of 2015." Avalanche Biotechnologies Inc., Annual Report (Form 10-K), 26 (Mar. 5, 2015).

238. However, less than two months after AVA-101 was determined to be ineffective in Phase 2a, Avalanche announced that it would not be proceeding with Phase 2b of the AVA-101 Trial in the second half of 2015. Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (Aug. 13, 2015). The decision to cease development based upon the poor efficacy results from Phase 2a is significant given that ***neither phase of the AVA-101 Trial was powered to demonstrate statistical significance as to efficacy***. Thus, the preliminary, un-blinded efficacy results were so negative that further development was not justified.

239. Thus, on this news, shares of Avalanche common stock dropped $3.82, or more than 27%, to close on August 14, 2015 at $10.01 per share.

240. On October 19, 2015, Avalanche announced that Linda Bain would resign from her position as CFO effective November 17, 2015. *See* Avalanche Biotechnologies, Inc., Current Report (Form 8-K) (Oct. 19, 2015).

VIII. CLASS PERIOD STATEMENTS AND EVENTS[34]

241. On or about May 30, 2014, Avalanche filed with the SEC its registration statement on Form S-1 (Registration No 333-197133). Following amendment, on July 30, 2014, the registration statement was declared effective by the SEC and Avalanche, the offering was priced at $17 per share. On July 31, 2014, the first day of the Class Period, Avalanche and the Individual Exchange Act Defendants filed the 2014 Prospectus with the SEC (the 2014 Prospectus was incorporated into the registration statement and together they formed the "2014 Registration Statement"), and sold 6,900,000 shares of common stock to the investing public for total proceeds of $106.8 million after deducting underwriting discounts, commissions, and expenses. The IPO was completed on August 5, 2014. Defendants Chalberg, Bain, Blumenkranz, and Schwartz, *inter alia*, signed the 2014 Registration Statement.

242. As described below, the 2014 Registration Statement contained untrue statements of material facts or omitted to state other facts necessary to make the statements made not misleading, and was not prepared in accordance with the rules and regulations regarding is preparation.

243. In regard to the study data received by the Company, Avalanche and the Individual Exchange Act Defendants stated in the 2014 Registration Statement:

> We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. ***Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated***. Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015.
>
> *** * ***

[34] The misleading or false portions of the Class Period statements have been emphasized in bold and italics or via other highlighting.

> We are currently conducting a Phase 2a trial for AVA-101 in wet AMD. ***Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015.***

244. The foregoing statements in ¶243 were materially false and/or misleading because the interim drug safety surveillance data ***also*** evidenced the following facts indicating that AVA-101 was ineffective in treating Wet AMD, which were omitted and/or misrepresented and were known or recklessly disregarded by the Exchange Act Defendants at the time of each statement:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 192-194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 192-194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

245. In regard to the durable effect of AVA-101, Avalanche and the Individual Exchange Act Defendants stated in the 2014 Registration Statement:

> In animal models, AVA-101 expression has been shown to last up to 17 months, and data from other studies with AAV in the retina have shown gene expression to last more than five years. ***In humans, AVA-101 has been studied up to one year, and we believe it has the potential to last much longer.***

246. In regard to the potential for AVA-101, Avalanche and the Individual Exchange Act Defendants stated in the 2014 Registration Statement:

> By contrast, AVA-101 is designed to enable retinal cells to continuously produce therapeutic levels of a naturally occurring anti-VEGF protein with a single administration. ***Accordingly, we believe that AVA-101 could transform the treatment paradigm and address a significant unmet need in this large wet AMD market***.

247. The foregoing opinions in ¶¶245-246 were either (1) false because the Exchange Act Defendants did not in fact believe the opinion based on their knowledge of the following adverse facts evidencing that AVA-101 was ineffective in treating Wet AMD; or (2) misleading because the

Exchange Act Defendants failed to disclose that they had not inquired into the following facts that were then available from the DMC:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

248. On October 16, 2014, defendant Chalberg presented on behalf of Avalanche at the Ophthalmology Innovation Summit at the American Academy of Ophthalmology 2014 Annual Meeting. The presentation contained the following slide:

249. The foregoing statements in ¶248 were materially false and/or misleading because they omitted and/or misrepresented the following adverse facts that existed at the time of each statement, which evidenced that AVA-101 was ineffective in treating Wet AMD, and were known or recklessly disregarded by the speaker at the time of each statement:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

250. On or about December 18, 2014, Avalanche filed with the SEC its registration statement on Form S-1 (Registration No 333-201388) for a secondary offering of common stock. Following amendment, on January 7, 2015 the registration statement was declared effective by the SEC and Avalanche and the underwriters priced the 2015 Offering at $59 per share. On January 7, 2015, Avalanche and the Individual Exchange Act Defendants filed the 2015 Prospectus with the SEC, and sold 2,399,457 shares of common stock, plus the underwriters' over-allotment of an additional 359,918 shares, to the investing public. The 2015 Offering was completed on January 13, 2015 and raised approximately $130.5 million. Defendants Chalberg, Bain, Blumenkranz, and Schwartz, *inter alia*, signed the 2015 Registration Statement.

251. In regard to the data viewed by the Company and the Individual Exchange Act Defendants, Avalanche, Chalberg, Bain, Blumenkranz, and Schwartz stated in the 2015 Registration Statement:

> We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. ***Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated.*** Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015.
>
> * * *

> We are currently conducting a Phase 2a trial for AVA-101 in wet AMD. ***Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015***.[35]

252. The foregoing statements in ¶251 were materially false and/or misleading because the interim drug safety surveillance data ***also*** evidenced the following facts indicating that AVA-101 was ineffective in treating Wet AMD, which were omitted and/or misrepresented and were known or recklessly disregarded by the speaker at the time of each statement:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 192-194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 192-194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

253. In regard to the durability of AVA-101, Avalanche, Chalberg, Bain, Blumenkranz, and Schwartz stated in the 2015 Registration Statement:

> In animal models, AVA-101 expression has been shown to last up to 17 months, and data from other studies with AAV in the retina have shown gene expression to last more than five years. ***In humans, AVA-101 has been studied up to one year, and we believe it has the potential to last much longer***.[36]

254. In regard to the potential of AVA-101, Avalanche, Chalberg, Bain, Blumenkranz, and Schwartz stated in the 2015 Registration Statement:

> By contrast, AVA-101 is designed to enable retinal cells to continuously produce therapeutic levels of a naturally occurring anti-VEGF protein with a single administration. Accordingly, ***we believe that AVA-101 could***

[35] These same statements was also made in the 3Q 2014 Form 10-Q dated November 12, 2014, the 2014 Form 10-K dated March 5, 2015, and the 1Q 2015 Form 10-Q dated May 13, 2015.

[36] This same statement was also made in the 2014 Form 10-K dated March 5, 2015.

> ***transform the treatment paradigm and address a significant unmet need in this large wet AMD market***.[37]

255. The foregoing opinions in ¶¶253-254 were either (1) false because the Exchange Act Defendants did not in fact believe the opinion based on their knowledge of the following adverse facts evidencing that AVA-101 was ineffective in treating Wet AMD; or (2) misleading because the Exchange Act Defendants failed to disclose that they had not inquired into the following facts that were then available from the DMC:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

256. In regard to the risks facing the Company at the time of the 2015 Offering, Avalanche, Chalberg, Bain, Blumenkranz, and Schwartz stated in the 2015 Registration Statement:

> ***Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.***
>
> * * *
>
> ***Successful continued development and ultimate regulatory approval of AVA-101 is critical for our future business success…***
>
> ***The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:***
>
> > ***we may not be able to provide evidence of efficacy and safety for AVA-101;***
> >
> > ***the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;***

[37] This same statement was also made in the 2Q 2014 Form 10-Q dated September 12, 2014, the 3Q 2014 Form 10-Q dated November 12, 2014, the 2014 Form 10-K dated March 5, 2015, and the 1Q 2015 Form 10-Q dated May 13, 2015.

* * *

[S]uccess in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing.

* * *

If our proprietary vectors are not shown to be safe and effective in targeting retinal tissue, we may not realize the value of our investment in directed evolution technology.

* * *

In addition, ***success in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing…***

We cannot be certain that any of our planned clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

* * *

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

> ***we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;***
>
> ***the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;***

* * *

The degree of market acceptance of our product candidates will depend on a number of factors, including:

> ***demonstration of clinical efficacy and safety compared to other more-established products;***

* * *

Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate is:

> ***safe, effective and medically necessary***;
>
> * * *
>
> ***All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities***.[38]

257. The foregoing risk factors in ¶256 were materially false and/or misleading because they omitted and/or misrepresented the following adverse facts that existed at the time of each statement, which evidenced that AVA-101 was ineffective in treating Wet AMD, and were known or recklessly disregarded by the speaker at the time of each statement:

a) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

258. On January 16, 2015, Piper Jaffray published a report summarizing its discussions with Avalanche management. In regard to the data from Phase 2a of the AVA-101 Trial, the report stated, in relevant part:

> The company is focused on 'managing expectations' for the 1H15 P2a data for AVA-101 in wet AMD and focusing on an emerging pipeline which it will highlight at its analyst event in March. Management notes they do know or see the P2a data, but are trying to contain expectations that the dramatic reduction in anti-VEGF antibody injection frequency in P1a may not be reproduced.

259. Shortly thereafter, Piper Jaffray issued a follow-up report to correct what it alleges it "erroneously wrote." The report stated that they meant to write that "'***management notes they do NOT know or see the data' for the 1H15 P2a AVA-101 wet AMD data***." The report then

[38] Substantially similar risk factors were also included in the 2Q 2014 Form 10-Q dated September 12, 2014, the 3Q 2014 Form 10-Q dated November 12, 2014, the 2014 Form 10-K dated March 5, 2015, and the 1Q 2015 Form 10-Q dated May 13, 2015.

reiterated that "***Management notes they don't know the data: The company is insistent that there is nothing they know about the trial which would change their views or expectations for the study***."

260. The foregoing statements in ¶259 were materially false and/or misleading because they omitted and/or misrepresented the following adverse facts that existed at the time of each statement, which evidenced that AVA-101 was ineffective in treating Wet AMD, and were known or recklessly disregarded by the speaker at the time of each statement:

a) As explained in ¶¶198 & 223, the Exchange Act Defendants unquestionably had access to the Phase 2a data as evidenced by the IOVS abstract published in June 2013;

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

c) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

261. Despite Piper Jaffray's and Avalanche's attempt at damage control, the damage was already done. On January 16, 2015, shares of Avalanche common stock dropped $3.19, or more than 6%, to close at $48.37 and never recovered above $50 again.

262. On March 5, 2015, Cowen and Company published a report summarizing the highlights from a lunch held with Chalberg and Bain. In regarding to Phase 2a of the AVA-101 Trial, the report stated in relevant part:

> The trial included an interim safety analysis which was conducted in June of 2014, several months after dosing in most patients. Management noted that this safety analysis was successfully passed, with no serious or worrisome adverse events detected. ***As the study is ongoing, management said that it does not have knowledge of any adverse event or efficacy data other that the safety data from the June 2014 safety analysis***. Nonetheless, management did say that the trial has a pharmacovigilance committee which monitors adverse events. Avalanche would be informed of any serious complications made known to the pharmacovigilance committee. Thus far the committee has not been notified of any serious adverse events in the trial. With nearly all patients at least nine months

> past their AVA-101 injection, we think this bodes well for AVA-101's safety profile in the Ph. IIa.

263. The foregoing statements in ¶262 were materially false and/or misleading because they omitted and/or misrepresented the following adverse facts that existed at the time of each statement, which evidenced that AVA-101 was ineffective in treating Wet AMD, and were known or recklessly disregarded by the speaker at the time of each statement:

a) As explained in ¶¶198 & 223, the Exchange Act Defendants unquestionably had access to the Phase 2a data as evidenced by the IOVS abstract published in June 2013;

b) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were experiencing significant thickening—not thinning—of the retinas; and

c) As explained in ¶¶156, 159, 160, 163, 164, 166-168, 170-178, 194, 199, 209-212, 223-228, 231-234, & 238, patients in Phase 2a of the AVA-101 Trial were requiring multiple rescue injections, evidencing that AVA-101 was not effective in treating Wet AMD.

264. At no point during the Class Period did the makers of these statements ever correct or update their statements.

IX. POST CLASS PERIOD EVENTS

265. After the market closed on June 15, 2015, Avalanche announced the top-line results from Phase 2a of its AVA-101 Trial. In regard to the primary endpoint, safety, the Company explained that Avalanche's "Phase 2a clinical study for AVA-101 met its 12-month primary endpoint, based on ophthalmic and systemic safety, demonstrating that AVA-101 was well tolerated with a favorable safety profile in subjects with wet age-related macular degeneration[.]" In regard to the secondary endpoints for Phase 2a, the Company revealed that AVA-101 was not effective and in some cases performed worse than the standards of care. Specifically, Avalanche stated:

> ***Overall, BCVA mean change from baseline did show a significant difference of 11.5 letters between the treatment (+2.2 letters) and control (-9.3 letters) groups (95 percent CI, 2.3-20.7 letters)***.
>
> More AVA-101 treated subjects improved or maintained stable vision (>-5 letters) with a low number (≤2) of rescue treatments. Specifically, 23.8 percent (treated) vs. 9.1 percent (control) maintained stable vision with ≤1

> rescue injections, and a significant number of AVA-101 treated subjects (42.9 percent) improved or maintained stable vision with ≤2 rescue injections compared with subjects in the control group (9.1 percent).
>
> BCVA improvement of ≥10 letters with ≤2 rescue injections was observed in 23.8 percent of treated subjects and 0 percent of subjects in the control group.
>
> ***The median number of rescue injections using the protocol-specified retreatment regimen was 2 (95 percent CI, 1-6 injections) in AVA-101 treated subjects compared with 4 (95 percent CI, 3-5 injections) in the control group***. More subjects required fewer retreatments in the treatment group compared with control (19.0 percent vs. 9.1 percent with 0 injections; 33.3 percent vs. 9.1 percent with ≤1 injections; 52.4 percent vs. 9.1 percent with ≤2 injections).
>
> ***Retinal thickness mean change from baseline***, as reported by the site using automated segmentation, ***was +25 µm for AVA-101 treated subjects compared with -56 µm in the control group*** (CI for the difference, 17 to 145 µm). Additional evaluation of SD-OCT images by an image reading center are ongoing.

266. Later that day the Company held a special conference call to discuss the top-line data and further reiterated several times that "the key takeaway is that this was a positive Phase 2a study that met its primary objective which was to further establish safety of AVA-101 in wet AMD patients and also help inform future studies going forward . . . we're very encouraged to also see that AVA-101 showed promising signs of efficacy[.]" However, the Company could not avoid the results showing that in regard to efficacy, Phase 2a utterly failed. The Company, Barone, and Chalberg stated the following:

> [Barone]: The primary endpoint was safety and tolerability of AVA-101 as measured by ophthalmic and/or systemic complications and laboratory tests. . . . The study met its primary endpoint. . . .
>
> [D]ata from secondary endpoints suggest evidence of biological activity in subjects treated with AVA-101. ***Overall, mean change in best corrected visual acuity from baseline showed a significant difference of 11.5 letters between the treatment group and gained 2.2 letters from baseline, compared to the control group which decreased 9.3 letters*** from baseline. The difference between groups had a 95% confidence interval of 2.3 letters to 20.7 letters.
>
> More AVA-101 treated subjects improved or maintained stable vision defined as a loss of less than five letters or any letter gain with a low number of rescue treatments defined as two or fewer. Specifically, 23.8% of treated subjects maintained stable vision with no more than one rescue injection versus 9.1% in the control group. ***And a significant number of AVA-101 treated subjects, 42.9%, improved or maintained***

> ***stable vision with no more than two rescue injections as compared to 9.1% of the subjects in the control group***.
>
> ***Best corrected visual acuity improvement of 10 letters or more with no more than two rescue injections was observed in 23.8% of treated subjects and 0% of the subjects in the control group***.
>
> ***The median number of rescue injections using the protocol-specific retreatment regimen was two in AVA-101 treated subjects compared to four in the control group***. More subjects required fewer retreatments in the AVA-101 group as compared to the control group. ***Specifically, 19.0% of treated subjects received zero injections versus 9.1% in the control group. 33.3% of treated subjects received one or fewer injections versus 9.1% in the control group. And 52.4% of treated subjects received two or fewer injections versus 9.1% in the control group***.
>
> ***Retinal thickness mean change from baseline, as reported by the site using automated segmentation, was plus 25 microns for AVA-101 treated subjects compared to minus 56 microns in the control group***. The confidence interval for the difference is 17 microns to 145 microns. Further OCT analysis will be undertaken using an image reading center.

267. Despite Chalberg's attempt to put a positive spin on this data, the market was not impressed. In an article entitled "Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club," one commentator stated that "I'm struggling to adequately describe the awfulness of Avalanche Biotechnologies' [] performance Monday night trying to explain and defend the mediocre results of its gene therapy study in wet age-related macular degeneration (AMD)." The author pointed out that when investors looked deeper at the results, they realized the flaws, concluding that "the painful lesson here is that Avalanche's study of AVA-101 may have achieved its primary efficacy endpoint, but the gene therapy failed the more important common sense endpoint." Adam Feuerstein, *Avalanche Fails Common-Sense Test, Kicked Out of Gene Therapy Credibility Club*, The Street (June 16, 2015), http://www.thestreet.com/story/13187351/1/avalanchefailscommonsensetestkickedoutofgenetherapycredibilityclub.html. Zacks called the data "lackluster" and "weak" explaining that "results disappointed investors[.]" *Avalanche Biotechnologies Slips on Weak AVA-101 Data*, Zacks Equity Research (June 16, 2015), http://www.zacks.com/stock/news/178460/avalanche-biotechnologies-slips-on-weak-ava101-data. An article published on investing website, the Motley Fool, explained

that "[t]he problem is that the retinas of patients receiving AVA-101 thickened relative to those in the control group, casting doubt on the gene therapy's efficacy as a treatment for wet AMD[,]" "one would expect the *exact* opposite result if AVA-101 was truly helping patients maintain their visual acuity." George Budwell, *Why Avalanche Biotechnologies, Inc. Stock Collapsed Today*, Motley Fool (June 16, 2015), http://www.fool.com/investing/general/2015/06/16/why-avalanche-biotechnologies-inc-stock-collapsed.aspx.

268. Accordingly, on this news shares of Avalanche common stock dropped $21.83, or more than 56%, to close on June 16, 2015 at $17.05 per share.

269. Also on June 16, 2015, William Blair downgraded Avalanche and moved its price target down to $24.00 from $53.00. *See* Tim Lugo, William Blair, *Lucentis Performance and Difficult Population Clouds Phase IIa; Phase IIb a Ways Away; Downgrading to Market Perform* (2015). SunTrust Robinson Humphrey also downgraded Avalanche and moved its price target down to $25.00 from $60.00. *See* Salveen Richter, SunTrust Robinson Humphrey, *Await Further AVA-101 Clarity, Lack of Near-Term Catalysts, DGrading to Neutral* (2015).

270. Throughout the Class Period, Avalanche and the Individual Exchange Act Defendants represented that after announcing the data from Phase 2a of the AVA-Trial in the middle of 2015, Avalanche planned to conduct Phase 2b of the AVA-101 Trial "in the second half of 2015" which would have been "a randomized, controlled, multi-center, double-masked study to assess the efficacy, safety and tolerability of a single subretinal injection of AVA-101 in [approximately 120] subjects with wet AMD." 2014 Form 10-K at 18.

271. Anticipation for the Phase 2b study, however, was short-lived. On August 13, 2015, after the market closed, Avalanche announced that it would not be conducting Phase 2b in the second half of 2015 or continuing its AVA-101 Trial program for Wet AMD due to the negative efficacy data from Phase 2a. Specifically, in a press release issued that day, the Company stated:

> The company also reported that after further analyses of results from a previously reported Phase 2a trial of AVA-101 for the potential treatment of wet age-related macular degeneration (wet AMD), ***it will not initiate a Phase 2b clinical trial in the second half of 2015***. Instead, Avalanche will conduct additional preclinical studies to investigate optimal dose and

> delivery of AVA-101 and AVA-201 versus standard of care Anti-VEGF protein therapy to select the best gene therapy product candidate for wet AMD to advance back to the clinic.

272. In the Form 10-Q for the quarter ended June 30, 2015 ("2Q 2015 Form 10-Q"), also filed on August 13, 2015, the Company explained that it had decided to abandon the AVA-101 Trial program because the results from Phase 2a of the Trial failed to show the desired effect, stating:

> ***Overall, we did not observe evidence of a complete and/or durable anti-VEGF response in the majority of subjects treated with AVA-101 as administered in the Phase 2a study. We are continuing to analyze the Phase 2a data in order to enhance our understanding of the study results with respect to the secondary endpoints and why we did not see a more complete, durable anti-VEGF response.*** To that end, we have decided not to move forward with the Phase 2b clinical trial for AVA-101 with the current dose and administration procedure that we had planned to initiate in the second half of 2015.

273. The decision to cease development based upon the poor efficacy results from Phase 2a is significant given that neither phase of the AVA-101 Trial was powered to demonstrate statistical significance as to efficacy. Thus, the preliminary, un-blinded efficacy results were so obviously negative that further development was not justified.

274. Thus, the market reacted negatively to this news, and shares of Avalanche common stock dropped $3.82, or more than 27%, to close on August 14, 2015 at $10.01 per share.

X. ADDITIONAL SCIENTER ALLEGATIONS

275. As alleged herein, the Exchange Act Defendants acted with scienter with respect to the Exchange Act Claims because at the time that they issued public documents and made other public statements in Avalanche's name, they knew or recklessly disregarded the fact that such statements were materially false and misleading and/or omitted material facts concerning the interim data for the AVA-101 Trial. Exchange Act Defendants (1) knew that such documents and statements would be issued or disseminated to the investing public, (2) knew that persons were likely to rely upon those misrepresentations and omissions, and (3) knowingly and/or recklessly participated in the issuance and/or dissemination of such statements and/or documents as primary violators of the federal securities laws. The Exchange Act Defendants' materially false and

misleading statements and omissions of material fact artificially inflated Avalanche's stock price during the Class Period.

A. Core Operations

276. Because the fraud alleged herein relates to the core business of Avalanche, knowledge of the facts underlying the fraud may be imputed to the Individual Exchange Act Defendants. *See Reese v. Malone*, 747 F.3d 557 (9th Cir. 2014). Indeed, Avalanche acknowledged in its 2014 Registration Statement that it has "not sold any products" and does "not expect to sell or derive revenue from any product sales for the foreseeable future" and therefore, its "business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed." 2014 Registration Statement at 12. Accordingly, the Individual Exchange Act Defendants, as senior level executives and/or directors at a company with only 18 full-time employees, were in such positions at the Company to access all material, non-public information concerning the interim data for the AVA-101 Trial. Thus, the Individual Exchange Act Defendants were well aware that the false or misleading statements detailed above about the data from the AVA-101 Trial and the intention to continue with Phase 2b, made contemporaneously with knowledge of contradictory information, were materially false and/or misleading when made.

277. The Individual Exchange Act Defendants clearly had access to the Company's trial protocols and procedures as well as interim data from the AVA-101 Trial because they discussed the relevant data in detail throughout the Class Period. In addition, the Individual Exchange Act Defendants repeatedly confirmed that they received interim safety surveillance data in June 2014. Even prior to the completion of Phase 2a of the AVA-101 Trial, the Individual Exchange Act Defendants would have had access to the ongoing results given that Avalanche collaborated with the LEI in developing and conducting the trial and the AVA-101 Trial was open-label, permitting access to the data at any time. ¶¶159-165. The Individual Exchange Act Defendants were also aware that investigators were testing visual acuity, retinal thickness, and leakage as part of the

safety analysis because they participated in the design of and sought regulatory approval for the AVA-101 Trial. ¶¶161, 162, 165-175. Finally, the members of Avalanche's Clinical Advisory Board and Scientific Advisory Board would have participated in designing the AVA-101 Trial and had access to and analyzed the data from the AVA-101 Trial. ¶¶159, 160.

B. Magnitude of the Fraud

278. The magnitude of the fraud provides additional support for the Exchange Act Defendants' scienter. At the time of the IPO, AVA-101 was the Company's only product in the clinical trial stage. 2014 Registration Statement at 1. During the Class Period, analysts projected that the peak year sales for AVA-101 by 2026 would be approximately $1.1 to $1.3 billion. *See* Biren Amin, Jefferies, *Avalanche Biotechnologies, Initiate Buy: AAVL Gene Therapy Has Disruptive Potential in Wet AMD*, 4 (2014); Tim Lugo, William Blair, *Avalanche Biotechnologies, Inc., Eyeing the Next Disruption in the AMD Market; Initiating Coverage with Outperform Rating and $52 Price Target*, 39 (2014). In 2014, Avalanched generated $572,000 in total revenue. *See* 2014 Form 10-K at 80. Thus the importance of the AVA-101 Trial to the Company and the massive impact approval would have on revenues suggests that the Exchange Act Defendants were aware of the safety/efficacy data which was freely available to them. *See Berson v. Applied Signal Tech., Inc.*, 527 F.3d 982, 988 n.5 (9th Cir. 2008).

C. The Individual Exchange Act Defendants' Experience

279. Moreover, each of the Individual Exchange Act Defendants were highly educated, trained, and experienced in drug development and ophthalmology and were therefore well aware that the so-called safety data necessarily included data relevant to AVA-101's efficacy. For example, Defendant Chalberg was highly educated and had extensive experience in ophthalmology research. Chalberg received an A.B. in Biochemical Sciences from Harvard University, a Ph.D. in Genetics from the Stanford University School of Medicine, and an M.B.A. from the Haas School of Business from the University of California, Berkeley. *See* 2014 Registration Statement at 103. Prior to co-founding Avalanche, Chalberg was a Howard Hughes Medical Institute Fellow at Stanford University, with research concentrations in retinal diseases and new gene therapy

technologies. *See id.* Chalberg went on to work at Genentech, a publically-traded biotechnology company, holding a number of positions as Market Development Senior Manager for Lucentis, an anti-VEGF therapy, and Avastin, as Group Manager for the Lucentis strategy team, and as Global Business Lead for Lucentis. *See id.* Chalberg co-founded Avalanche in 2006, had served on the Board of Directors since then, and began his tenure as the Company's President and CEO in October 2010. *See id.*

280. Defendant Bain is a Certified Public Accountant, who received a B.S. in Accounting and Business Administration and an Honors Degree in Accounting and Business Administration from the University of the Free State in South Africa. *See id.* Prior to joining Avalanche, Bain worked at Bluebird Bio, a gene therapy biotechnology company, as a Chief Accounting Officer, Treasurer, and VP of Finance and Business Operations. *See id.* Bain has also served in positions with Genzyme, a biotechnology company, with AstraZeneca, a publicly-traded pharmaceutical company, and as VP at Fidelity Investments. *See id.* Bain joined Avalanche in April 2014, as CFO and Treasurer. *See id.*

281. Defendant Blumenkranz is also highly educated and has extensive experience in ophthalmology research and practice. Dr. Blumenkranz received his A.B. in Biology, his M.M.S. in Biochemical Pharmacology, and his M.D. from Brown University. *See id.* Dr. Blumenkranz then followed his medical education with a residency in ophthalmology at Stanford University. *See id.* Dr. Blumenkranz is an experienced vitreoretinal surgeon and is the current Chairman of the Department of Ophthalmology at the Byers Eye Institute at Stanford University. *See id.* Dr. Blumenkranz also serves on a number of boards of directors for privately held biotechnology companies, including, Vantage Surgical Systems Inc., Oculogics, Inc., Presbia Holdings, Digisight Technologies Inc. and Oculeve, Inc. *See id.* Prior to co-founding Avalanche, Dr. Blumenkranz served on the faculty of the Bascom Palmer Eye Institute in Miami, Florida. *See id.* From October 1985 to August 1992, Dr. Blumenkranz founded and served as Director of the Vitreoretinal Fellowship Program at William Beaumont Hospital in Royal Oak, Michigan. *See id.* From 2000 to 2004, Dr. Blumenkranz served on the scientific advisory board of Eyetech, a biopharmaceutical

company. *See id.* Dr. Blumenkranz co-founded Avalanche in 2006, and has served on its board of directors since its inception.

282. Defendant Schwartz also has experience and expertise in ophthalmology research and practice. Dr. Schwartz received his B.A. from the University of California, Berkeley, his M.D. from the Keck School of Medicine at the University of Southern California, followed by a Residency in Ophthalmology at the University of California, Los Angeles, and a vitreoretinal fellowship at Moorefield's Eye Hospital in London. *See id.* at 105. Dr. Schwartz is currently an ophthalmologist and vitreoretinal surgeon, as well as the Ahmanson Professor of Ophthalmology at the Jules Stein Eye Institute at the University of California, Los Angeles. *See id.* Prior to co-founding Avalanche, he served as the principal investigator for a number of early-stage clinical trials for retinal diseases, including studies for ranibizumab (Lucentis), as well as products in gene and cell therapy. *See id.* Dr. Schwartz also held various positions at Eyetech, a biopharmaceutical company, and currently serves on the board of directors of the American Society of Retina Specialists. *See id.* Dr. Schwartz has also served on a number of scientific advisory boards for numerous biotechnology and ophthalmology technology companies. Dr. Schwartz co-founded Avalanche in 2006, and has served on its board of directors since September 2010. *See id.*

D. Financial Motives of the Avalanche Insiders

283. While in possession of negative safety/efficacy data, indicating that Phase 2a of the AVA-101 Trial was not having an anti-VEGF affect in patients, Avalanche launched its IPO on July 31, 2014, selling 6,900,000 shares for total proceeds of $106.8 million. *See* Avalanche Biotechnologies, Inc., Press Release (Form 8-K) (Aug. 5, 2014).

284. Then, after sufficiently hyping the results from Phase 1 of the AVA-101 Trial and still failing to disclose the negative safety/efficacy results from Phase 2a, Avalanche launched a second public offering on January 7, 2015, selling 2,759,375 shares of common stock for proceeds of $130.5 million. *See* Avalanche Biotechnologies, Inc., Press Release (Form 8-K) (Jan. 13, 2015).

285. According to Forms 4 filed with the SEC by Avalanche insiders, the Individual Exchange Act Defendants and certain members of the Avalanche Board of Directors took

advantage of inside information regarding known Phase 2a efficacy data, and made stock sales that were highly suspicious in both timing and amount.

286. ***Chairman of the Board of Directors Mark Blumenkranz***: Between January 13, 2015 and June 11, 2015, Blumenkranz sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sales Price	Proceeds
1/13/2015	100,000	$55.46	$5,546,000.00
4/7/2015	21,774	$38.58	$840,040.92
	726	$39.06	$28,357.56
	2,904	$38.58	$112,036.32
	96	$39.06	$3,749.76
4/8/2015	2,500	$39.93	$99,825.00
4/16/2015	24,800	$41.58	$1,031,184.00
	200	$42.04	$8,408.00
5/1/2015	20,000	$32.36	$647,200.00
5/11/2015	1,785	$34.91	$62,314.35
5/13/2015	715	$34.94	$24,982.10
5/15/2015	17,975	$35.36	$635,596.00
	4,525	$35.99	$162,854.75
5/19/2015	3,000	$36.91	$110,730.00
6/5/2015	5,000	$40.08	$200,400.00
6/9/2015	15,300	$35.52	$543,456.00
	7,000	$36.20	$253,400.00
	200	$37.35	$7,470.00
6/10/2015	600	$39.91	$23,946.00
6/11/2015	1,900	$39.97	$75,939.20

287. In a five-month span, Blumenkranz sold a total of 231,000 shares of Avalanche common stock at an average price of $38.69 per share, for total proceeds of approximately $10,417,890.[39] The proceeds amounted to approximately 243 times the annual director fees he

[39] It does not appear as though Avalanche provided a cost basis for the shares held by its executives in its SEC filings because it is an Emerging Growth Company as defined by the JOBS Act. *See* 2014 Registration Statement at 5. Accordingly, Plaintiffs have only included the insiders' proceeds from these sales.

earned during the year ended December 31, 2014.[40] Furthermore, Blumenkranz' sales during the Class Period constituted approximately 20% of his common stock holdings.[41] Blumenkranz has not sold a single share of Avalanche common stock since the Class Period ended.

288. ***Director Steven Schwartz***: Between January 13, 2015 and June 15, 2015, Schwartz sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sales Price	Proceeds
1/13/2015	91,000	$55.46	$5,046,860.00
4/9/2015	17,050	$39.71	$677,055.50
	200	$40.37	$8,074.00
4/23/2015	16,875	$38.61	$651,543.75
5/8/2015	17,250	$33.04	$569,940.00
5/22/2015	11,679	$38.15	$445,553.85
	5,196	$38.88	$202,020.48
6/1/2015	14,157	$36.10	$511,067.70
	3,093	$36.81	$113,853.33
6/15/2015	16,875	$39.86	$ 672,637.50

289. In a five-month span, Schwartz sold a total of 193,375 shares of Avalanche common stock at an average price of $39.70 per share, for total proceeds of approximately $9,000,000. The proceeds amounted to 360 times the annual director fees he earned during the year ended December 31, 2014. Furthermore, Schwartz's sales during the Class Period constituted approximately 18% of his common stock holdings. Schwartz has also not sold a single share of Avalanche common stock since the Class Period ended.

290. ***Former CEO Thomas W. Chalberg***: Between January 13, 2015 and June 10, 2015, Chalberg sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sales Price	Proceeds

[40] Annual director fees were derived from the "Non-Employee Director Compensation" section on page 22 of Avalanche's Schedule 14A Proxy Statement, filed with the SEC on April 30, 2015.

[41] Common stock holdings were derived from the "Security Ownership of Certain Beneficial Owners and Management" section on page 30 of the Avalanche Schedule 14A Proxy Statement, filed with the SEC on April 30, 2015.

1/13/2015	85,000	$55.46	$4,714,100.00
5/5/2015	25,000	$30.00	$750,000.00
6/10/2015	5,035	$36.88	$185,690.80
	12,970	$38.03	$493,249.10
	6,995	$38.90	$272,105.50

291. In a five-month span, Chalberg sold a total of 135,000 shares of Avalanche common stock at an average price of about $40 per share, for total proceeds of approximately $6,415,145. Furthermore, Chalberg's sales during the Class Period constituted approximately 7% of his common stock holdings. The proceeds amounted to approximately 16 times the annual salary earned in the year ended December 31, 2014. Chalberg has also not sold a single share of Avalanche common stock since the Class Period ended.

292. ***Senior VP of Business Operations Hans Hull***: Between April 7, 2015 and June 4, 2015, Hans Hull ("**Hull**") sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sales Price	Proceeds
4/7/2015	26,613	$38.58	$1,026,729.54
	887	$35.44	$31,438.24
5/4/2015	5,000	$30.87	$154,350.00
6/4/2015	2,000	$37.64	$75,283.20

293. In a short two-month span, Hull sold a total of 34,500 shares of Avalanche common stock at an average price of $35.63 per share, for total proceeds of approximately $1,287,801. The proceeds amounted to approximately 5 times the annual salary he earned during the year ended December 31, 2014.[42] Furthermore, Hull's sales during the Class Period constituted approximately 39% of his common stock holdings. Hull has not sold a single share of Avalanche common stock since the Class Period ended.

[42] Annual salary was derived from the "Executive and Director Compensation" section on page 112 of Avalanche's Form S-1 Registration Statement, filed with the SEC on January 1, 2015.

294. ***Director Paul Wachter***: Between January 13, 2015 and June 15, 2015, Wachter sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sale Price	Proceeds
1/13/2015	14,000	$55.46	$776,440.00
4/13/2015	830	$39.09	$32,444.70
	338	$39.84	$13,465.92
	24	$40.74	$977.76
4/20/2015	1,192	$40.19	$47,906.48
4/27/2015	1,192	$35.60	$42,435.20
5/4/2015	1,192	$30.86	$36,785.12
5/11/2015	508	$32.79	$16,657.32
	552	$33.70	$18,602.40
	132	$34.29	$4,526.28
5/18/2015	1,192	$35.30	$42,077.60
5/26/2015	786	$36.51	$28,696.86
	304	$37.59	$11,427.36
	102	$38.29	$3,905.58
6/1/2015	982	$36.11	$35,460.02
	210	$36.81	$7,730.10
6/8/2015	541	$37.96	$20,536.36
	475	$38.95	$18,501.25
	176	$39.88	$7,018.88
6/15/2015	1,192	$39.86	$47,513.12

295. In a five-month span, Wachter sold a total of 25,920 shares of Avalanche common stock at an average price of approximately $38 per share, for total proceeds of approximately $1,213,108. The proceeds amounted to approximately 58 times the annual director fees he earned during the year ended December 31, 2014. Furthermore, Wachter's sales during the Class Period constituted approximately 29% of his common stock holdings. Wachter has not sold a single share of Avalanche common stock since the Class Period ended.

296. ***Senior VP of Pharmaceutical Development Mehdi Gasmi***: Between April 7, 2015 and June 15, 2015, Medhi Gasmi ("**Gasmi**") sold thousands of shares of Avalanche common stock, as set forth in the following chart:

Trade Date	Number of Shares Sold	Sale Price	Proceeds
4/7/2015	8,708	$38.58	$335,954.64
	292	$39.06	$11,405.52
4/14/2015	1,000	$39.44	$39,440.00
4/21/2015	1,000	$39.21	$39,210.00
4/28/2015	1,000	$35.67	$35,667.00
5/7/2015	500	$33.27	$16,635.00
5/14/2015	500	$35.31	$17,655.00
5/21/2015	500	$38.87	$19,435.00
5/28/2015	500	$38.01	$19,005.00
6/8/2015	235	$37.96	$8,920.60
	183	$38.95	$7,127.85
	82	$39.88	$3,270.16
6/15/2015	500	$39.86	$19,930.00

297. In a short two-month span, Gasmi sold a total of 15,000 shares of Avalanche common stock at an average price of approximately $38 per share, for total proceeds of approximately $573,659. The proceeds amounted to approximately twice his annual salary during the year ended December 31, 2014. Furthermore, Gasmi's sales during the Class Period constituted approximately 34% of his common stock holdings. Gasmi has not sold a single share of Avalanche common stock since the Class Period ended.

298. ***Former CFO Linda Bain***: Between May 4, 2015 and June 12, 2015, Bain sold thousands of shares of Avalanche common stock as set forth in the following chart:

Trade Date	Number of Shares Sold	Sale Price	Proceeds
5/4/2015	2,500	$31.58	$78,950.00
5/11/2015	715	$34.91	$24,960.65
5/13/2015	285	$34.94	$9,957.90
6/12/2015	3,500	$39.94	$139,790.00

299. In a very brief one-month span, Bain sold a total of 7,000 shares of Avalanche common stock at an average price of $35.34 per share, for total proceeds of approximately $253,659. Bain has not sold a single share of Avalanche common stock since the Class Period ended.

300. While Avalanche and the Individual Exchange Act Defendants repeatedly insisted to the public that the only Phase 2a data they had received was interim drug "safety" data in June 2014, the Individual Exchange Act Defendants along with the other Avalanche executive listed above, sold a combined total of 641,795 shares of Avalanche common stock, for combined proceeds of over $29,059,865—more than 25% of the proceeds Avalanche obtained in the IPO—in a span of only five months, with the heaviest trading (55% of shares sold) occurring 70 days prior to the release of the Phase 2a efficacy results. Furthermore, the average percentage of holdings sold during the five month period, across the Individual Exchange Act Defendants and Avalanche executives listed above, was approximately 14%.

301. The timing of the above-mentioned insider sales creates a strong inference of scienter. Most of the sale dates (97%) fall in the 70 day window leading up to the Company's Phase 2a results announcement, with almost every insider noted above selling a few days before the Company announced its Phase 2a results.

302. Many of the insiders' sales noted above occurred successively—often within days of their prior sales—and occurred in a short window of time. Some of the insiders' sales occurred on overlapping dates. For example, on April 7, 2015, Blumenkranz, Hull, and Gasmi all sold shares, while on May 4, 2015, Hull, Wachter and Bain all sold shares. Furthermore, as indicated above, none of the insiders sold shares after the announcement of the disappointing Phase 2a data.

303. Most of the insiders noted above sold at an average sale price of approximately $38-$40 per share, only a few dollars under the peak price of approximately $42 per share both in mid-April and mid-June, after the trading lock-up period came to a close in early April 2015.

304. Furthermore, Blumenkranz, Chalberg, Schwartz, and Wachter all took advantage of the one exception in the lock-up period imposed by the IPO and sold thousands of shares in the 2015 Offering. Also, the 2015 Offering imposed an additional lock-up period of 90 days following. Accordingly, when the lock-up periods finally came to a close on April 7, 2015, the Avalanche insiders soon after began an onslaught of trades, with a number of insiders trading that same day and almost every insider selling a significant number of shares in April 2015. It is well known that

insiders sales through a public offering to avoid the restrictions of a lock-up period are suspicious. See When insiders sell in a secondary offering, it is often an indication that "they see problems on the horizon." Dan Caplinger, *Secondary Offerings: What You Need to Know*, Motley Fool, (Feb. 25, 2013); Jonathan Weil, *Don't Buy When IPO Insiders Rush to Sell*, BloombergView (Mar. 26, 2014, 12:53 PM) (if insiders are "so eager to be selling, you probably don't want to be buying.").

E. Officer Resignations

305. On July 23, 2015, shortly after the topline results from Phase 2a were released, Chalberg announced his resignation as CEO and president and member of the Board of Directors. *See* Avalanche Biotechnologies, Inc., Press Release (Form 8-K) (July 23, 2015).

306. It was highly suspicious for the CEO who founded the Company, helped develop AVA-101, and has a long-standing relationship with LEI to resign in the middle of Phase 2 testing. Furthermore, Chalberg was not paid any severance and was instead kept on at Avalanche as a consultant and Scientific Advisor for one year. *See* Avalanche Biotechnologies, Inc., Press Release (Form 8-K) (July 23, 2015).

307. Then, on October 19, 2015, shortly after the Company decided not to continue with a Phase 2b trial, CFO Linda Bain notified the Company of her intention to resign.

308. There was no reason provided for Chalberg and Bain's resignations. Drug trial failures are not uncommon; the fact that the CEO and CFO resigned after such a failure alone is highly suspicious.

F. Duty to Monitor

309. Pursuant to TGA and FDA regulations, as the sponsor of the AVA-101 Trial, Avalanche was under a duty to monitor the accumulating safety data during the Trial. *See* ¶¶179-182; TGA GCP Guide at §5.16.1; 21 C.F.R. § 312.32(b); 21 C.F.R. § 312.56(c).

310. A defendant is reckless when they have "failed to review or check information that they had a duty to monitor, or ignored obvious signs of fraud." *N.M. State Inv. Council v. Ernst & Young LLP*, 661 F.3d 1089, 1098 (9th Cir. 2011).

311. Either the Exchange Act Defendants monitored the safety data as they were required to do, and thus were aware that AVA-101 was not effective in patients in Phase 2a of the AVA-101 Trial, or the Exchange Act Defendants failed to carry out this duty to monitor, willfully ignoring the data available from the DMC and acting with deliberate recklessness.

G. As Agents Rakoczy's and Constable's Knowledge May Be Imputed to Avalanche

312. "[T]he Ninth Circuit [] recognizes respondeat superior liability for a corporation under 10(b) and 10b-5 based on common law agency principles." *In re Hienergy Techs., Inc.*, 2005 U.S. Dist. LEXIS 47044, at *23 (C.D. Cal. Oct. 24, 2005); *Hollinger v. Titan Capital Corp.*, 914 F.2d 1564, 1578 (9th Cir. 1990) (In 10b-5 cases, "the principal who acts through the agent (assuming the agent is acting within the scope of his agency) is secondarily liable"). Thus, the securities fraud context, "[t]he scienter of the" agents "of a corporation may be attributed to the corporation itself to establish liability as a primary violator of § 10(b) and Rule 10b-5" when those agents were acting within the scope of their apparent authority. *In re ChinaCast Educ. Corp. Sec. Litig.*, 809 F.3d 471, 476 (9th Cir. 2015).

313. As members of the Scientific Advisory Board and Clinical Advisory Board, Rakoczy and Constable, respectively, were agents of Avalanche.

314. Constable was the Principal Clinical Investigator and performed the subretinal injections on each patient. He was also responsible for all aspects of the participants' welfare and clinical data interpretation, and supervising the collectors of clinical data and imaging. Rakoczy as an investigator was responsible for liaising with clinical, statistical, and research staff, data management and interpretation, and liaising with patients if necessary. Both Rakoczy and Constable reviewed the interim data collected during Phase 1 of the AVA-101 Trial and were named on the trial abstracts discussing the data. They are also both named in the June 2013 IOVS abstract that discussed Phase 2a safety data for 9 patients. Due to these roles, in addition to the fact that the AVA-101 Trial was not blinded to the investigators, Rakoczy and Constable would have been aware during the Class Period that AVA-101 was not having an anti-VEGF affect in patients

in Phase 2a. Indeed, they would have known which patients received the subretinal injection and they would have been aware of when those patients were receiving rescue injections. As Avalanche's agents, Rakoczy's and Constable's knowledge of these facts can be imputed to Avalanche.

H. The Exchange Act Defendants' Concealment

315. "Evidence of concealment is strongly indicative of scienter." *Brown v. China Integrated Energy, Inc.*, 875 F. Supp. 2d 1096, 1124 (C.D. Cal. 2012) ("The allegation indicates the fact that China Integrated knew its representations about its biodiesel production was false, and attempted to ensure that investors would not discover this fact by taking steps to make it appear that the facility was functioning at full capacity."); *see In re Nuvelo*, 668 F. Supp. 2d 1217, 1231 (N.D. Cal. 2009) (finding that "the SAC allege[s] that defendants concealed known risks of failure that, if disclosed, would have reduced the price of Nuvelo's stock to account for the greater risk of failure[,]" and therefore, the "SAC satisfie[s] the scienter element."); *In re Boeing Sec. Litig.*, 40 F. Supp. 2d 1160, 1175 (W.D. Wash. 1998) (inferring scienter when "defendants concealed Boeing's production problems so that the price of Boeing stock would remain high enough to make the merger attractive").

316. The Exchange Act Defendants took several steps to conceal the fact that AVA-101 was having a negative effect on Trial patients.

317. The Exchange Act Defendants inconsistently reported the Trial data—choosing only to report more data when it benefited their narrative such as the positive data in the first 8 patients of the Phase 1 portion of the AVA-101 Trial. *See* Ex. D, Trial Overview; Ex. H, April 2014 Abstract (including detailed information on, inter alia, visual acuity, retinal thickness, and the number of rescue injections given). Yet, the Exchange Act Defendants did not release information with this level of detail for Phase 2a until the end of the Class Period.

318. As part of their concealment, whenever the Exchange Act Defendants would discuss the Trial's status they would omit the endpoint data which they had no previous aversion to reporting—choosing only to report that the "interim drug safety surveillance data" indicated

only that AVA-101 was "well tolerated[,]" (2014 Registration Statement), when the data showed more.

319. In order to keep investors in the dark on the data, the Exchange Act Defendants never disclosed the fact that the three measures used to determine three safety endpoints were also the three measures used to determine the secondary efficacy endpoint. *See* ¶¶124, 175, *supra*. During a lunch with analysts, Charlberg and Bain went out of their way to avoid discussing this issue, telling a group of analysts that they "did not have knowledge of any adverse event or efficacy data other tha[n] the safety data from the June 2014 safety analysis." Phil Nadeau, Cowen & Co., Highlights from Lunch with Management, 1 (Mar. 5, 2015).

320. In fact, by the Exchange Act Defendants' own admission, they had looked at some of the Phase 2a data, as set forth in the June 2013 IOVS abstract.

XI. LOSS CAUSATION

321. During the Class Period, as detailed herein, the Exchange Act Defendants engaged in a fraud to deceive the market in a way that artificially inflated Avalanche's stock price and operated as a fraud or deceit on Class Period purchasers of Avalanche stock by misrepresenting the Company's business and prospects. During the Class Period, the Exchange Act Defendants misrepresented and concealed the negative efficacy data from the AVA-101 Trial. As a result of their purchases of Avalanche stock during the Class Period at artificially inflated prices, the Exchange Act Plaintiff and other Exchange Act Class members suffered damages as the true facts and Avalanche's fraud were revealed.

322. The Exchange Act Defendants' wrongful conduct, as alleged herein, directly and proximately caused the damages suffered by the Exchange Act Plaintiff and Exchange Act Class.

323. The Exchange Act Defendants' false and misleading statements and omissions in their SEC filings and other public statements during the Class Period directly caused losses to the Exchange Act Plaintiff and Exchange Act Class. On the strength of these false statements, the Company's stock price was artificially inflated to a Class Period high of $60.08 per share on January 7, 2015. Those misrepresentations and omissions that were not immediately followed by

an upward movement in the Company's stock price served to maintain the share price at artificially inflated levels by maintaining and supporting a false positive perception of Avalanche's business, operations, performance, and prospects.

324. As the truth began to emerge regarding the adverse patient data from AVA-101, the price of Avalanche's stock declined as the market processed each set of previously undisclosed facts. Each such disclosure removed a portion of the artificial inflation in the price of Avalanche's common stock and directly and proximately caused the Exchange Act Plaintiff and other Exchange Act Class members to suffer damages. For example, On June 16, 2015, shares of Avalanche common stock closed at $17.05 per share, a 56% decline on unusually heavy volume. Then, on August 14, 2016 shares of Avalanche common stock dropped $3.82, or more than 27%, to close at $10.01 per share.

325. Until shortly before the Exchange Act Plaintiff filed this Complaint, he was unaware of the facts alleged herein and could not have reasonably discovered the Exchange Act Defendants' misrepresentations and omissions by the exercise of reasonable diligence.

XII. CONTROL PERSON LIABILITY

326. The Individual Exchange Act Defendants are liable as direct participants with respect to the wrongs complained of herein. In addition, the Individual Exchange Act Defendants, by reason of their status as senior executive officers and/or directors, were "controlling persons" within the meaning of Section 20(a) of the Exchange Act, and each had the power and influence to cause the Company to engage in the unlawful conduct complained of herein. Because of their positions of control, the Individual Exchange Act Defendants were able to and did, directly or indirectly, control the conduct of Avalanche's business.

327. Specifically, because of their positions within the Company, the Individual Exchange Act Defendants possessed the power and authority to control the contents of Avalanche's SEC filings, annual and quarterly reports, press releases, and presentations to securities analysts, money and portfolio managers and institutional investors, *i.e.*, the market, including those containing the materially false and misleading statements and omissions of material fact alleged

herein. Each of the Individual Exchange Act Defendants, by reason of his/her respective management or board position, had the ability and opportunity to review copies of the Company's SEC filings, reports, press releases, and other statements alleged herein to be misleading, prior to, or shortly after their issuance or to cause them to be corrected.

328. By virtue of their positions, the Individual Exchange Act Defendants had access to material non-public information. Each of the Individual Exchange Act Defendants knew or recklessly disregarded the fact that the adverse facts specified herein had not been disclosed and were being concealed from the public, and that the positive representations which were being made were then materially false and misleading.

XIII. APPLICABILITY OF THE FRAUD ON THE MARKET DOCTRINE

329. The market for Avalanche's common stock was an efficient market for the following reasons, among others:

a) Avalanche's common stock was listed and actively traded on the NASDAQ, a highly efficient national market;

b) As a registered and regulated issuer of securities, Avalanche filed periodic reports with the SEC, in addition to the frequent voluntary dissemination of information;

c) Avalanche regularly communicated with public investors through established market communication mechanisms, including through regular dissemination of press releases on the national circuits of major newswire services and through other wide-ranging public disclosures such as communications with the financial press and other similar reporting services;

d) Avalanche was followed by multiple analysts, which followed Avalanche's business and wrote reports which were publicly available and affected the public marketplace;

e) The material misrepresentations and omissions alleged herein would tend to induce a reasonable investor to misjudge the value of Avalanche's stock; and

f) Without knowledge of the misrepresented or omitted facts, the Exchange Act Plaintiff and other members of the Exchange Act Class purchased Avalanche stock between the time the Exchange Act Defendants made the material misrepresentations and omissions and the time that the truth was revealed, during which time the price of Avalanche stock was artificially inflated by the Exchange Act Defendants' misrepresentations and omissions.

330. As a result of the above, the market for Avalanche securities promptly digested current information with respect to the Company from all publicly available sources and reflected such information in the security's price. The historical daily trading prices and volumes of Avalanche's publicly traded stock are incorporated by reference herein. Under these circumstances, many purchasers of Avalanche common stock during the Class Period suffered similar injuries through their purchases of shares at prices which were artificially inflated by the Exchange Act Defendants' misrepresentations and omissions. Thus, a presumption of reliance applies.

XIV. THE AFFILIATED UTE PRESUMPTION

331. The Exchange Act Plaintiff is entitled to a presumption of reliance under *Affiliated Ute Citizens of Utah v. United States*, 406 U.S. 128 (1972), because the claims asserted herein against the Exchange Act Defendants are predicated primarily on omissions of material fact which the Exchange Act Defendants had a duty to disclose. Under *Affiliated Ute*, all that is necessary is that the facts withheld be material in the sense that a reasonable investor might have considered them important in making a decision to purchase or sell the securities. *Id.* at 153-54. Here, the Exchange Act Defendants had a duty but failed to disclose, at the time of issuance, material facts regarding poor Phase 2a efficacy data. These facts would have been important to a reasonable investor, as part of Avalanche's success depends on the outcome of its clinical trials.

XV. NO SAFE HARBOR

332. The safe harbor provisions for forward-looking statements under the Private Securities Litigation Reform Act of 1995 are applicable only under certain circumstances that do

not apply to any of the materially false and misleading statements and omissions alleged in this Complaint.

333. First, many of the identified false and misleading statements and omissions herein are not forward-looking statements, but instead are statements of current or historic fact.

334. Second, to the extent there were any forward-looking statements that were identified as such at the time made, there were no meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the purportedly forward-looking statements.

335. Third, such false and misleading statements were not accompanied by cautionary language that was meaningful because any such warnings or "risk" factors contained in, or incorporated by reference in, the relevant press release, SEC filings, earnings class, or other public statements described herein were general, "boilerplate" statements of risk that would affect any pharmaceutical development company, and misleadingly contained no factual disclosure of any of the specific details of the endemic problems affecting the Company during the Class Period, or similar important factors that would give investors adequate notice of such risks.

336. Fourth, to the extent there were any forward-looking statements that were identified as such at the time made, the Exchange Act Defendants are liable for those false and misleading forward-looking statements because at the time each of those forward-looking statements was made, the particular speaker knew that the particular forward-looking statement was false, or, by reason of what the speaker failed to note, was materially false and/or misleading, and/or that each such statement was authorized and/or approved by a director and/or executive officer of Avalanche who actually knew that each such statement was false or misleading when made.

XVI. CLAIMS FOR RELIEF UNDER THE EXCHANGE ACT

COUNT III

For Violations of Section 10(b) of the Exchange Act and Rule 10b-5 Against The Exchange Act Defendants

337. The Exchange Act Plaintiff re-alleges each allegation set forth above in the Exchange Act Claims section as if fully set forth herein.

338. This claim is brought under Section 10(b) of the Exchange Act (15 U.S.C. § 78j(b)) and Rule 10b-5 promulgated thereunder by the SEC (17 C.F.R. § 240.10b-5), against the Exchange Act Defendants.

339. During the Class Period, the Exchange Act Defendants violated Section 10(b) of the Exchange Act and Rule 10b-5(b) promulgated thereunder by making the false and misleading statements specified herein, including the statements in SEC filings, presentations, press releases, and analyst reports concerning the data for the AVA-101 Trial reviewed by the Exchange Act Defendants, whose truth they knowingly or recklessly disregarded when they failed to disclose material facts necessary to make the statements made, in light of the circumstances under which they were made, not false and misleading.

340. The Exchange Act Defendants, individually and in concert, directly and indirectly, by the use, means or instrumentalities of interstate commerce and/or the mails, engaged and participated in a course of conduct to conceal non-public, adverse material information about the Company's operations and financial condition as reflected in the misrepresentations and omissions set forth above.

341. The Exchange Act Defendants each had actual knowledge of the misrepresentations and omissions of material facts set forth herein, or acted with deliberately reckless disregard for the truth by failing to ascertain and to disclose such facts even though such facts were available to them, or deliberately refrained from taking steps necessary to discover whether the material facts were false or misleading.

342. As a result of the Exchange Act Defendants' dissemination of materially false and misleading information and their failure to disclose material facts, Plaintiffs and the Class Members

were misled into believing that the Company's statements and other disclosures were true, accurate, and complete.

343. Avalanche is liable for the acts of the Individual Exchange Act Defendants and other Company personnel referenced herein under the doctrine of respondeat superior, as those persons were acting as the officers, directors, and/or agents of Avalanche in taking the actions alleged herein.

344. The Exchange Act Plaintiff and the Exchange Act Class members purchased Avalanche common stock, without knowing that the Exchange Act Defendants had misstated or omitted material facts about the Company's operations and financial performance or prospects. In so doing, the Exchange Act Plaintiff and Exchange Act Class members relied directly or indirectly on false and misleading statements made by the Exchange Act Defendants, and/or an absence of material adverse information that was known to Defendants or recklessly disregarded by them but not disclosed in the Exchange Act Defendants' public statements. The Exchange Act Plaintiff and Exchange Act Class members were damaged as a result of their reliance on the Exchange Act Defendants' false statements and misrepresentations and omissions of material facts.

345. At the time of the Exchange Act Defendants' false statements, misrepresentations and omissions, the Exchange Act Plaintiff and Exchange Act Class members were unaware of their falsity and believed them to be true. The Exchange Act Plaintiff and Exchange Act Class would not otherwise have purchased Avalanche common stock had they known the truth about the matters discussed above.

346. The Exchange Act Plaintiff is filing this action within two years after discovery of the facts constituting the violation, including facts establishing scienter and other elements of the Exchange Act Plaintiff's claims, and within five years after the violations with respect to the Exchange Act Plaintiff's investments.

347. By virtue of the foregoing, the Exchange Act Defendants have violated § 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder.

348. As a direct and proximate result of the Exchange Act Defendants' wrongful conduct, the Exchange Act Plaintiff the relevant members of the Class have suffered damages in connection with their purchase of Avalanche common stock.

COUNT IV

For Violations of Section 20(a) of the Exchange Act Against the Individual Exchange Act Defendants

349. The Exchange Act Plaintiff realleges each allegation set forth in the Exchange Act Claims section above as if fully set forth herein.

350. This Count is asserted against the Individual Exchange Act Defendants for violations of Section 20(a) of the Exchange Act, 15 U.S.C. § 78t(a), on behalf of all members of the Exchange Act Class.

351. As set forth above, Avalanche committed a primary violation of Section 10(b) of the Exchange Act by knowingly and/or recklessly disseminating materially false and misleading statements and/or omissions throughout the Class Period.

352. Each of the Individual Exchange Act Defendants, by reason of their status as senior executive officers and/or directors of Avalanche, directly or indirectly, controlled the conduct of the Company's business and its representations to the Exchange Act Plaintiff and the Exchange Act Class, within the meaning of §20(a) of the Exchange Act. The Individual Exchange Act Defendants directly or indirectly controlled the content of the Company's SEC statements and press releases related to the Exchange Act Plaintiff's and the Exchange Act Class' investments in Avalanche common stock within the meaning of §20(a) of the Exchange Act. Therefore, the Individual Exchange Act Defendants are jointly and severally liable for the Company's fraud, as alleged herein.

353. The Individual Exchange Act Defendants controlled and had the authority to control the content of the Company's SEC statements and press releases. Because of their close involvement in the every-day activities of the Company, and because of their wide-ranging supervisory authority, the Individual Exchange Act Defendants reviewed or had the opportunity to

review these documents prior to their issuance, or could have prevented their issuance or caused them to be corrected.

354. The Individual Exchange Act Defendants knew or recklessly disregarded the fact that Avalanche's representations were materially false and misleading and/or omitted material facts when made. In so doing, the Individual Exchange Act Defendants did not act in good faith.

355. By virtue of their high-level positions and their participation in and awareness of Avalanche's operations and public statements, the Individual Exchange Act Defendants were able to and did influence and control Avalanche's decision-making, including controlling the content and dissemination of the documents that the Exchange Act Plaintiff and Exchange Act Class contend contained materially false and misleading information and on which the Exchange Act Plaintiff and Exchange Act Class relied.

356. The Individual Exchange Act Defendants had the power to control or influence the statements made giving rise to the securities violations alleged herein, and as set forth more fully above.

357. As set forth above, Avalanche committed a primary violation of Section 10(b) of the Exchange Act by knowingly and/or recklessly disseminating materially false and misleading statements and/or omissions throughout the Class Period as well as by omitting the adverse patient data from the investing public.

358. As a direct and proximate result of the Individual Exchange Act Defendants' wrongful conduct, the Exchange Act Plaintiff and the relevant members of the Class suffered damages in connection with their purchase of Avalanche common stock.

XIV. PRAYER FOR RELIEF

WHEREFORE, the Exchange Act Plaintiff on behalf of himself and the relevant members of the Class, prays for relief and judgment including:

A. Determining that Counts III through IV of this action are a proper class action under Federal Rules of Civil Procedure 23, certifying the Exchange Act Plaintiff as Class representative

under Rule 23 of the Federal Rules of Civil Procedure, and certifying the Exchange Act Plaintiffs' counsel as Class Counsel;

B. Awarding compensatory damages in favor of the Exchange Act Plaintiff and the other Class members against all Exchange Act Defendants, jointly and severally, for all damages sustained as a result of the Exchange Act Defendants' wrongdoing, in an amount to be determined at trial, including pre-judgment and post-judgment interest, as allowed by law;

C. Awarding rescissory damages in favor of the Exchange Act Plaintiff and the other Class members where appropriate against all of the Exchange Act Defendants, jointly and severally, for all injuries sustained as a result of the Exchange Act Defendants' wrongdoing, in an amount to be determined at trial, including pre-judgment and post-judgment interest, as allowed by law;

D. Awarding extraordinary, equitable, and/or injunctive relief as permitted by law (including, but not limited to, rescission);

E. Awarding the Exchange Act Plaintiff and the Class their costs and expenses incurred in this action, including reasonable counsel fees and expert fees; and

F. Awarding such other and further relief as may be just and proper.

JURY TRIAL DEMAND

Plaintiffs hereby demand a trial by jury on all triable claims.

Dated: December 2, 2016

FARUQI & FARUQI, LLP

By: */s/ Richard W. Gonnello*

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CERTIFICATE OF SERVICE

I hereby certify that on December 2, 2016, I authorized the electronic filing of the foregoing with the Clerk of the Court using the CM/ECF system which will send notification of such filing to the e-mail addresses denoted on the attached Electronic Mail Notice List.

By: */s/ Richard W. Gonnello*
Richard W. Gonnello

Mailing Information for a Case 3:15-cv-03185-JD In re Avalanche Biotechnologies Securities Litigation

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Manual Notice List

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- (No manual recipients)